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EDITORIAL

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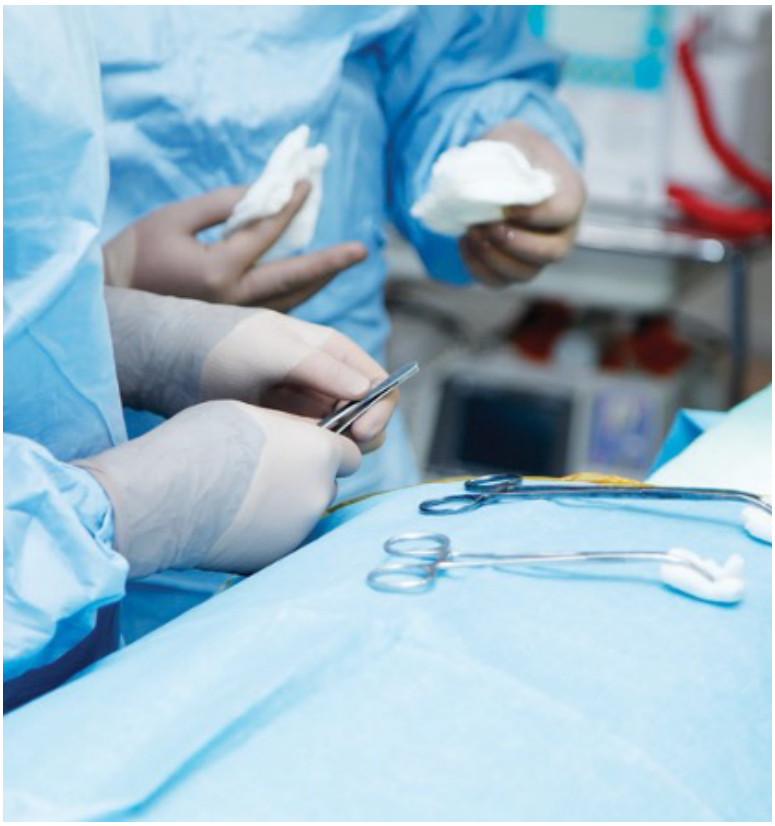

SURGERY AND TRANSPLANTATION

The key activities of these departments of NSMC are reconstructive surgery, transplantation, innovative minimally invasive approaches, microsurgical correction, cell-based therapy of various surgical diseases.
New types of minimally invasive surgical technologies, video-endoscopic and microsurgical techniques, mini-thoracoscopic operations, chemoembolization of tumors were implemented that fundamentally change the approaches to the treatment of many surgical diseases and reduce the time of hospitalization of the patients.

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The Problem with Permanent Expressions of Concern: Perpetual Doubt

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Abstract

The expression of concern (EoC) evolved in the neoliberal corrective culture of science to represent an "alert system" for potential problems with papers that might arise at the post-publication stage. One of the problems with EoCs is that they may take months or even years to resolve, while some EoCs remain as such forever. Fairly recently, Elsevier, a publishing giant, introduced a new form of EoCs, or rather, the plain EoC morphed into two types, the temporary EoC, and the permanent EoC. The permanent EoC leaves that paper in a permanent state of unknown use and unclear reliability.

Key words: corrections; literature integrity; misconduct; retractions; transparency.

To the Editor,

Academics, as the grassroots level of the publishing industry, are expected to appreciate how the world of publishing is evolving, for better or for worse. This is because trends and changes will surely impact their research and publication journey. One salient transformation in this academic generation is the cultural shift towards corrective measures. In academic publishing, available procedures to correct the literature are still rigid, or at least insufficiently flexible to accommodate evolving trends of doubt, error, or misconduct, limited primarily to corrigenda or errata, expressions of concern (EoCs), and retractions [1]. For this reason, given peer review's imperfections make literature susceptible to critique at the post-publication stage, a double digital object identifier (DOI)-based method of publication was suggested, in which the second DOI would be a "live" document that would emerge, allowing for the publishing record to be updated at any time in the history of the article's existence, serving as a transparent and effective corrective measure [2].

As we witness and participate in a growing culture of retractions, it is important to observe and critique, and in doing so, seek to improve corrective measures that have the ability to impact scientists, through citations [3]. Since a citation essentially reflects dependence on ideas, facts, or methodologies, the reliability or veracity of the cited document becomes central in publishing. It is incumbent upon academics, as active members of the publication process, to critique policies that may ultimately impact them. As one example, concern was previously expressed about the "clustering" of multiple EoCs into a single DOI-based notice rather than a one EoC to one paper ratio [4]. While such a process is undoubtedly convenient to publishers when faced with mass doubt or fraud, it undermines the transparency of the process.

EoCs have typically come to serve as a temporary "warning" to readers or potential users of that paper that some issue(s) may be impacting its scientific (or other) integrity. However, if unfounded, that state of uncertainty can harm the authors of papers to which an EoC is attached, robbing them of the possibility of being cited. Conversely, potential users of papers associated with an EoC may be hesitant to cite that work. This dual harm is amplified when EoCs remain endlessly in an unresolved state. Surely, in such a situation, the double-DOI system of publication that adopts a more neutral stance, but that offers greater transparency and details about the process [2], would benefit academics more?

Elsevier, as one of the giants in the status quo publishing ecosystem, in some ways represents a trail-blazer because it adapts its practices to meet the cultural challenges of the moment. Given its legal prowess (Elsevier and LexisNexis, a law firm, are under the same umbrella parent company RELX), academics need to pay close attention to tweaks in the publishing culture made by Elsevier (and other status quo publishers) because

they may ultimately affect them, directly or indirectly. At some point, Elsevier introduced a new form of EoCs, or rather, the plain EoC morphed into two types, the temporary EoC, and the permanent EoC [5]. The precise date of this new "cultural" form of the correction of the literature is unknown since Elsevier (unfortunately) has not dated its document. Three known examples are noted [6-8]. To the author's knowledge, no such dual-purpose EoC exists yet for other publishers, nor has such terminology been indicated formally by ethics organizations like COPE or the ICMJE.

In my opinion, the permanent EoC leaves that literature in a permanent state of unknown use and unclear reliability. While this decision may offer the editors, journal and publisher legal refuge – because sufficient self-protecting caution is exercised – it prolongs the agony of not knowing the intellectual destiny of that work. Surely academics prefer clarity and resolution to constant doubt? Unless of course, a permanent state of doubt is meant to introduce a Cartesian tint to the state of science, suggesting that the underlying knowledge is false, but always tending on a trajectory to appreciate its state of truth [9]. If the perception of "reasonable doubt" [10] were to be applied, while accepting the fallibility of knowledge, then it is possible to envision that a wide swathe of published literature might need to have an EoC attached to it, given human imperfections that populate science and academia.

In some ways, publishing is not unlike the social and geopolitical trends that we are witnessing, and in many respects is influenced by and is susceptible to them. Academics are usually marginalized – because they are not included in policy-making – by tectonic shifts in policies, especially those that relate to ethics, and are thus at the whim of decisions made by publishers and their legal departments, or ethics organizations that cement such policies globally, usually autocratically. Surely, in this day and age of diversity, inclusivity and equity, is it not advisable for publishers to consult and interact with a wider span of the academic base before deciding and implementing policies that may merely add a layer of complexity without necessarily resolving core issues?

In my assessment, the permanent EoC brings no added value to the culture of knowledge correction. Instead, editors and publishers need to be much more decisive, acting on available evidence, but not leaving academic works (and their authors) in a permanent state of uncertainty and anxiety [11, 12].

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Current Trends in Radiological Diagnostics and Treatment of the Temporal Bone Pyramid Pathologies

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Abstract

Diseases of the middle ear and the temporal bone pyramid remain among the most common diseases in the structure of otorhinolaryngological pathologies, significantly impacting the quality of patients' life. Exudative processes and their consequences become one of the main causes of persistent hearing loss and are characterized by an asymptomatic course. Timely and complete diagnosis and high-quality follow-up are leading to preventing the development of conductive hearing loss and other complications.

Purpose of the study. To study the main predisposing factors, methods of radiological diagnosis, and dynamic observation of patients, as well as some modern aspects of treating the most common pathologies of the temporal bone pyramid.

Methodology. We analyzed open-access sources from scientific databases such as Scopus, PubMed, Google Scholar, Web of Science, DisserCat, and CyberLeninka. Keywords used for the search: "chronic otitis media," "cholesteatoma," "mastoiditis," "complications," "magnetic resonance imaging," "DWI," and "computed tomography." Publications included in the literature review were full-text articles in English and Russian and dissertations in Russian. Exclusion criteria: brief reports, newspaper articles, and personal communications. The search range was five years (2018-2023). A total of 114 sources were analyzed, of which 48 met the research objectives and inclusion criteria.

Results and conclusions. In diagnosing temporal bone pathologies, computed tomography is the gold standard for diagnosis, but non-ionizing research techniques such as magnetic resonance imaging are increasingly used. In treating complicated diseases, endoscopic and laser correction methods are used in foreign practice, helping to reduce the risk of recurrence and postoperative complications.

Keywords: chronic otitis media, cholesteatoma, magnetic resonance imaging, computed tomography, treatment.

Introduction

Diseases of the middle ear and the pyramid of the temporal bone are among the most serious diseases in the ENT (Ear, nose and throat) stage, which significantly impact the quality of life of adults and children. Exudative processes and their consequences become one of the main causes of persistent hearing loss and are characterized by low-symptomatic forms with a gradual evolution to chronic forms. It should be noted that in childhood, the risk of disorders of speech and intellectual development increases, leading to psycho-emotional effects, social maladaptation of the child, and a decrease in the quality of life. The most common diseases of the temporal bones are chronic otitis media, middle ear cholesteatoma, and mastoiditis. At the same time, these cases are now increasingly found in pediatric practice, which is associated with untimely provision of outpatient otorhinolaryngological care. Timely and complete diagnosis and high-quality follow-up play a leading role in preventing the development of conductive hearing loss and other complicated pathologies of the temporal bone pyramids.

Methodology

The purpose of the study was to study predisposing factors, modern methods of radiological diagnosis and dynamic monitoring of patients, as well as some modern aspects of treatment of the most common pathologies of the temporal bone pyramids. We analyzed open sources based on scientific databases Scopus, Google Scholar, PubMed, DisserCat, Web of Science, and CyberLeninka. Keywords used for the search: "chronic otitis media," "cholesteatoma," "mastoiditis," "magnetic resonance imaging," "DWI," and "computed tomography." Publications included in the literature reviews were full-text articles in English and English, as well as abstracts in English. Exclusion criteria: brief reports, newspaper articles, and personal communications. Depth was looking for a career for five years (2019-2023). One hundred eight sources were analyzed, of which 50 included research objectives and inclusion criteria.

Search results and their analysis

Predisposing factors

Chronic otitis media is a heterogeneous condition characterized by persistent inflammation of the middle ear and/or mastoid cavity, widespread in both adult and pediatric populations. Common symptoms of this disease include otorrhea, hearing loss, and dizziness [1,2]. Worldwide, people with moderate to profound hearing loss increased from 225.3 million in 1990 to 403.3 million in 1990. It is predicted that by 2050, 2.45 billion (2.35–2.56) people will have hearing loss, an increase of 56.1% from 2019 [3]. Chronic otitis media can be divided into chronic suppurative otitis media and chronic otitis media with cholesteatoma formation [4]. The most common causes of otitis media are:

1) changes in the mucous membrane of the auditory tube due to acute diseases of the nose, paranasal sinuses, and nasopharynx as a result of a decrease in general immunity;

2) Eustachian tube dysfunction;

3) anatomical and physiological features of the development of the auditory tube in childhood;

4) rhinitis of an allergic nature;

5) ineffective therapy for acute otitis media;

6) blockage of the mouth of the Eustachian tube with adenoid vegetations;

7) benign and malignant formations of the nasopharynx [1,4].

In the context of the sources studied some particular causes of the development of chronic otitis media can be identified. In the pathogenesis of eosinophilic otitis media, the leading role is played by a history of bronchial asthma, which is explained by the similar histological structure of the walls of the middle ear and bronchi [5,6]. Andreeva G.A. reports the establishment of a high correlation between the occurrence of complicated forms of exudative otitis media in children born with a median cleft palate [7]. A study by Youngrak Jung et al. suggests an increased risk of developing otitis media and hearing impairment in patients after total laryngectomy and gastrostomy tube placement [8]. The above examples indicate that impaired swallowing and, as a consequence, Eustachian tube dysfunction are predictors of the development of chronic otitis media and its complications. The literature provides some examples of the influence of atypical flora in the occurrence of exudative otitis media. While receiving immunosuppressive therapy, otitis media complicated by Bell's palsy was caused by mycoplasma hominis in a patient with a history of multiple sclerosis [9]. In this regard, when selecting antibiotic therapy in the treatment of protracted forms of otitis media, clinicians need to remember the possible impact of atypical flora in conditions of immunosuppression.

The term cholesteatoma was first used in a case report in 1838 to describe a "tumor" presumably composed of cholesterol and fat (chole- for cholesterol, steate- for fat, and -oma for tumor) [10]. Cholestatoma is often a complication of long-term chronic otitis media. It is localized in the middle ear with possible spread to the mastoid process, which is surrounded by critical intracranial structures, the involvement of which can cause serious neurological complications (facial palsy, labyrinthine fistula, brain abscess, and sigmoid sinus thrombosis). Cholesteatoma has locally destructive growth, which can lead to conductive hearing loss. In rare cases, cholesteatoma can cause sensorineural hearing loss when it spreads to the inner ear [10].

Cholesteatoma is often secondary, but primary (congenital) forms also occur. Secondary cholesteatoma most often develops against the background of chronic inflammation of the middle ear, less frequently the paranasal sinuses, as a result of the transfer of stratified squamous epithelium, which produces keratin, to areas where this tissue is not usually present. Secondary cholesteatoma can also be iatrogenic, associated with inadequately performed revision of the tympanic cavity, especially after repeated radical operations on the ear, forming a large trepanation cavity. [eleven]. The main, and often the only symptom of iatrogenic cholesteatoma is progressive hearing loss. Thus, in a case observation from Anikin I.A., in a patient with repeated sanitizing operations on both ears and complaints of hearing loss, according to MRI (magnetic resonance imaging), a giant cholesteatoma of the mastoid process measuring 34x37x30.4 mm with extension to the posterior cranial fossa and compression of the hemisphere was discovered cerebellum [12]. In some cases, the development of cholesteatoma is induced by trauma. J. Ajduk reports a case of cholesteatoma, which was discovered and removed from a patient 29 years after receiving a gunshot wound to the head, in which the bullet passed through the left mastoid process and the cavity of the inner ear. The patient underwent reconstructive surgery, and almost three decades later, when the patient complained of otorrhea and hearing loss, an MRI revealed cholesteatoma of the mastoid process. [13]. Scott Mayer and co-authors established a significant relationship between the occurrence of chronic otitis media and exudative otitis and cholesteatoma in patients with Langerhans cell histiocytosis, which is presumably due to the lytic nature of the lesions of all skeletal bones in this pathology [14]. There are rare examples in the literature describing cholesteatoma of the paranasal sinuses, confirmed by biopsy. According to CT (computed tomography) data, cholesteatoma had a nonspecific picture and was defined as a total shadowing of the frontal sinus of heterogeneous density, destroying the wall of the orbit [15].

Congenital cases of cholesteatoma are extremely rare. Congenital cholesteatoma results from improper formation of the ectoderm rudiment in the early stages of embryogenesis [16]. Congenital cholesteatomas are diagnosed more often in children under three years of age. Severe congenital concomitant pathology is a risk factor for the occurrence of congenital cholesteatoma and also contributes to the unfavorable course of the process. According to a study by Chernogaev E.A., congenital cholesteatoma is most often observed in children with severe neurological pathology as part of congenital syndromes. Congenital cholesteatomas are bilateral [17]. There is a belief that cholesteatoma in children has a more aggressive growth than in adults: the well-pneumatized mastoid processes in children contribute to more extensive damage compared with the more sclerotic mastoid processes in adults [18].

Mastoiditis develops when the infection spreads into the cells of the mastoid process. Mastoiditis most often occurs as a complication of untreated acute or chronic otitis media caused by an infection of the middle ear.

Radiological diagnostics: current trends

Radiation research methods in diagnosing middle ear diseases in otorhinolaryngological departments are used not only as a method of standard primary diagnosis but also as a mandatory point in preoperative preparation. The "golden" preoperative standard is a computed tomography scan of the temporal bones [19]. Otosurgeons rely on CT scans as an anatomical and structural map before surgery. However, the use of CT is not always appropriate in acute clinical conditions, such as acute mastoiditis in children. The usefulness of temporal bone CT in trauma evaluation may also be limited. Temporal bone fractures usually don't require urgent surgical intervention in the absence of complete facial paralysis. Carrying out CT scans in young children involves anesthesia, which is associated with certain risks, especially in children with severe symptoms of intoxication due to purulent-destructive processes [21]. Moreover, the use of general anesthesia with hardware support is recommended only after fasting for 4-5 hours, which may delay the start of surgery and increase the risk of intracranial complications. Thus, although CT of the temporal bones is an essential method of X-ray examination in acute processes, its use requires additional evaluation due to the peculiarities of pediatric practice. A detailed assessment of temporal bone pathology may not be necessary for clinical decision-making and nonsurgical management. In addition, according to Kosyakov et al., CT makes it challenging to differentiate cholesteatoma with granulations, fibrous changes, and inflammatory and purulent contents [22].

There is evidence of the use of dual-energy CT, which represents a promising imaging tool in patients with contraindications to MRI. At a cost and relatively low radiation exposure, DECT (dual energy computed tomography) is a cheaper, faster examination with the added benefit of providing high-resolution anatomical detail [22].

In modern practice, clinicians tend to minimize studies with ionizing radiation. The MRI technique has become an integral addition to computed tomography data in the preoperative period, and in cases of diagnosing intracranial complications and long-term dynamic monitoring of patients, MRI confidently occupies a leading position in foreign practice. Venous sinus thrombosis as a complication of acute mastoiditis was encountered in a case series by Eleni Vergadi et al. [23]. At the same time, neurological symptoms predominated in children, and when they worsened, patients underwent MRI and MR venography of the brain. Subsequently, according to MRI data, signs of venous sinus thrombosis were revealed in 5 out of 20 patients, which played a leading role in further treatment tactics.

Various MRI techniques utilizing diffusion-weighted imaging (DWI) are employed for cholesteatoma detection. DWI captures the random motion of water molecules within tissue, known as Brownian motion. While free water molecules exhibit constant random motion due to thermal kinetic energy, the movement of water molecules within cellular environments is constrained by interactions with cellular structures like cell walls and organelles. This restriction correlates with tissue cellularity levels. DWI proves particularly valuable in tumor and cerebral ischemia diagnosis. Cholesteatoma detection on DWI images has a threshold of 2–3 mm. On MRI-DWI sequences with a b-value of 1000, cholesteatomas appear as hyperintense signals, notably brighter than brain parenchyma, especially within surrounding cerebrospinal fluid, facilitating easy identification. DWI MRI is pivotal in staging cholesteatomas larger than 5 mm and assessing the presence of granulation tissue. The DWI PROPELLER sequence, utilized in high-field MRI systems abroad, is extensively employed in temporal bone cholesteatoma diagnosis. Based on a multiple fast spin echo (FSE) technique, this sequence mitigates B0-related artifacts and enhances signal intensity by periodically rotating parallel lines during each repetition period. It diminishes blur typical in single-shot and fast spin echo sequences with a relatively short echo time, while its b-value of 1500 heightens diffusion sensitivity with a slight signal-to-noise ratio reduction.

Recent research has highlighted the significance of MRI in identifying indications of inflammation within the temporal bone, including its deterioration. During acute mastoiditis, MRI can reveal bone structures more distinctly due to intramastoid mucosal edema and inflammatory exudation, which displace air, generating a high-intensity background for the signal-cavity bone structures on T2-weighted images. Moreover, contrast enhancement and restricted diffusion of mastoid contents are probable indicators of the extent of mastoid inflammation [28]. For the purpose of postoperative assessment and diagnosis of possible complications, CT is the method of choice for assessing the condition of the ossicular chain and incus-stapedius joint, and contrast-enhanced MRI is preferable when assessing soft tissue anatomical structures after removal of expansive lesions, incl. cholesteatoma [29]. In addition, the leading role of DWI MRI is emphasized for dynamic monitoring to exclude recurrence and residual lesions. After extensive open debridement

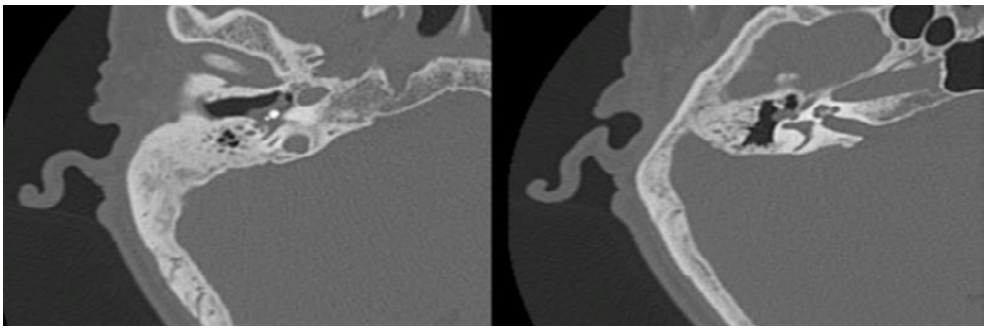

Figure 1 – Computed tomograms of the temporal bones, axial projection. Condition after cochlear implantation on the right. CT signs of right-sided otitis media with cholesteatoma and signs of osteolysis of the auditory ossicles

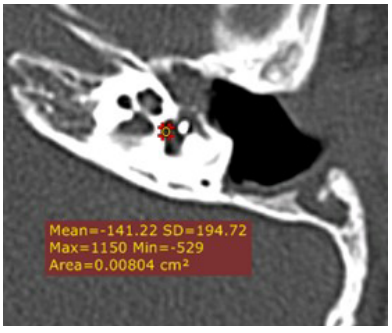

Figure 2 – Computed tomograms of the temporal bones, axial view. Condition after stapedectomy and stapedoplasty. Cholesteatoma masses of the tympanic cavity

operations for temporal bone cholesteatoma, the risk of recurrence remains. This fact dictates the need for regular long-term monitoring of this group of patients in the postoperative period.

The invasive nature of cholesteatoma growth, its prolonged asymptomatic phase, and the potential for intracranial complications underscore the need for routine, repeated middle ear MRI scans in DWI mode during the postoperative period to promptly detect relapse. Delrue et al. conducted a study examining the long-term outcomes of subtotal petrosectomy with blind external auditory canal closure for extensive cholesteatoma and chronic suppurative otitis media, utilizing diffusion-weighted magnetic resonance imaging (DWI MRI) for clinical and diagnostic follow-up. Out of 48 patients, seven exhibited residual cholesteatoma, with an average interval of 3.7 years between surgery and detection. Among those with chronic suppurative otitis media, three patients had residual cholesteatoma, detected on average 4.5 years post-surgery. This highlights DWI MRI's effectiveness in early detecting recurrent cholesteatoma, owing to its non-invasiveness and high resolution. Consequently, many experts advocate for CT and MRI assessments of temporal bone pathologies, with MRI being prioritized for long-term follow-up due to its comprehensive and dependable imaging capabilities

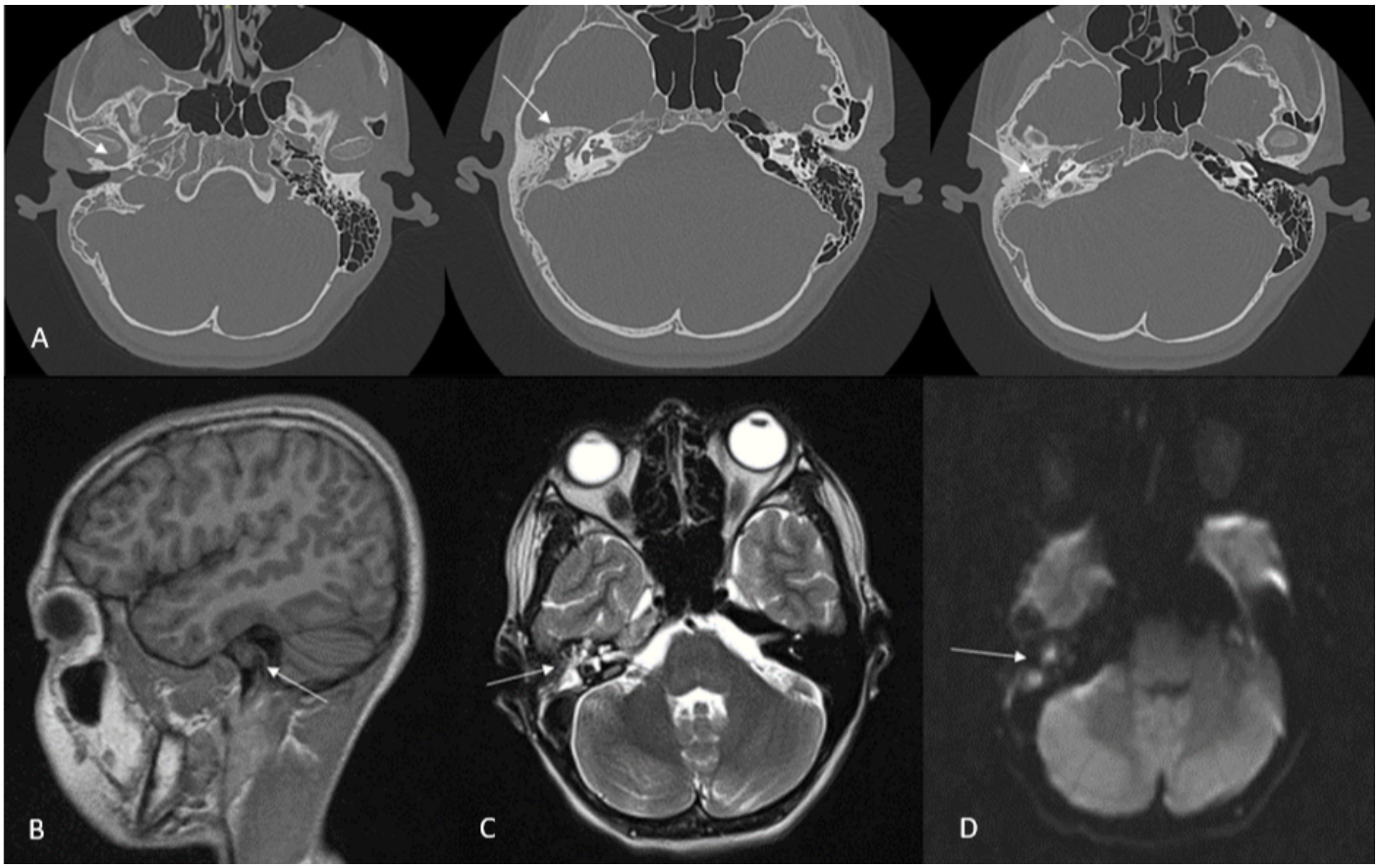

Figure 3 – Computer and magnetic resonance tomograms of the temporal bones of a 15-year-old patient with complaints of unilateral hearing loss on the right, frequent episodes of otitis media. A – Computer tomograms of the temporal bones in the axial projection. In the external auditory canal, parietal contents are determined. The mastoid process, antrum and attic are filled with pathological contents, the contours of the mastoid cells have marginal erosions. The density of the auditory bones is reduced, the incus has uneven contours. CT signs of external and otitis media on the right with signs of osteolysis of the auditory ossicles. To exclude the presence of cholesteatoma masses, MRI in DWI mode is recommended. The same patient, B – magnetic resonance imaging in T1-VI mode, sagittal projection, C – T2-VI mode, axial projection, D – DWI mode (b-1000), axial projection. In the area of the antrum and attic, against the background of increasing signal intensity on T2-VI, focal formations are determined, moderately hyperintense in the T2-VI mode (B), isointense in the T1 mode (A), irregular in shape with unclear uneven contours, moderately heterogeneous structure, these formations limit diffusion on DWI (b-1000) (C), confirming the presence of cholesteatoma masses in the middle ear cavity

In the external auditory canal, parietal contents are determined. The mastoid process, antrum and attic are filled with pathological contents, the contours of the mastoid cells have marginal erosions. The density of the auditory bones is reduced, and the incus has uneven contours. CT signs of external and otitis media on the right with signs of osteolysis of the auditory ossicles. MRI in DWI mode is recommended to exclude the presence of cholesteatoma masses.

The same patient, B - magnetic resonance imaging in T1-VI mode, sagittal projection, C - T2-VI mode, axial projection, D - DWI mode (b-1000), axial projection. In the area of the antrum and attic, against the background of increasing signal intensity on T2-VI, focal formations are determined: moderately hyperintense in the T2-VI mode (B), isointense in the T1 mode (A), irregular in shape with unclear uneven contours, moderately heterogeneous structure, these formations limit diffusion on DWI (b-1000) (C), confirming the presence of cholesteatoma masses in the middle ear cavity.

Radiological diagnostics: additional techniques

Fusion of DWI MRI and CT images has been reported in studies in which high signal intensity cholesteatoma lesions on

DWI MRI were superimposed on corresponding CT temporal bone structures to improve preoperative detection, evaluation, and localization of cholesteatoma. The " fusion " technology of diffusion-weighted MRI and CT images allows us to determine the localization of MR hyperintense cholesteatoma within the bony anatomical details obtained on CT. This improves the diagnosis of the presence and precise localization of cholesteatoma. Diffusion-weighted MRI/CT fusion combines the advantages of detecting residual cholesteatoma and determining its exact location [22]. A preoperative CT scan performed before the first surgery can be used for fusion with non-EPI (non-echo planar imaging) DWI to spare the patient unnecessary repeat CT scans and thus reduce radiation exposure [32]. Combined DW-T1W-CT imaging is a reliable tool for detecting cholesteatoma (sensitivity 92%, specificity 90%, and overall accurate predictive value 91.4% [33]. It is also useful for preoperative assessment of the cholesteatoma extent, which is critical for determining patient suitability for transcanal endoscopic middle ear surgery and assisting in surgical planning and patient consultation [33].

In addition to radiological diagnostic methods, doctors from the otorhinolaryngological service have proposed a faster, less expensive and non-invasive analogue, tympanometric measurement of middle ear volume, as a preoperative research method [34]. Since the degree of pneumatization of the mastoid process is a kind of “buffer” of pressure for the middle ear, it can be taken as a prognostically favorable factor in the effectiveness of the upcoming tympanoplasty. Temporal bone CT is the primary method for assessing mastoid aeration. However, due to radiation risks and the cost of the test, there is a need for a simpler, faster, and more reliable method in uncomplicated cases of chronic otitis media. For this purpose, it has been proposed that tympanometric volume measurements be used during tympanometry. When assessing the study results, it was found that the tympanometry volume values increased with an increase in the degree of aeration of the mastoid process. This shows the proportional relationship between the degree of mastoid pneumatization and the tympanometry volume measurement [34].

Specific cases

Tuberculous otitis media, a rare manifestation of extrapulmonary tuberculosis, constitutes a mere 0.1% of all tuberculosis cases and ranges from 0.04% to 0.9% of chronic suppurative otitis media cases [35]. Its pathogenesis typically involves contiguous spread via the Eustachian tube, hematogenous dissemination from the lungs or distant organs, or direct inoculation through the external auditory canal and tympanic membrane perforation. Clinical presentation often features the classic triad: painless otorrhea, multiple eardrum perforations upon otoscopic examination, and hearing impairment. However, its nonspecific symptoms often lead to misdiagnosis, resulting in treatment delays. Timely identification and intervention are crucial to prevent complications such as hearing loss, mastoiditis, labyrinthitis, osteomyelitis, abscess formation, and central nervous system involvement. In adults, the disease remains poorly understood, with clinical suspicion heightened by a history of tuberculosis, though cases without such history also occur [36].

Tuberculous otitis media may be overlooked when patients primarily present with otologic symptoms, especially given its rarity and insidious nature. Suspicion should arise in patients with suspected tuberculosis history or chronic otitis media in tuberculosis-endemic areas [37]. Histopathological examination of biopsy specimens offers a definitive diagnosis, often prompting surgical intervention for symptom relief. Prolonged tuberculous otitis media can result in complications like perforation, substantial hearing loss, and facial nerve paralysis, necessitating histological examination for accurate diagnosis in refractory chronic otitis cases. HE. Barkanova, provides a clinical observation demonstrating a rare manifestation of extrapulmonary tuberculosis in one ear in a patient without immunodeficiency, but with a previous history of pulmonary tuberculosis with residual changes in them. The patient's prolonged purulent otitis for 1.5 years was considered nonspecific, and only surgical intervention with histological analysis of the surgical material made it possible to establish the tuberculous nature of the process [38].

In a case series of tuberculous mastoiditis among children, all cases exhibited acute bacterial mastoiditis symptoms, with notable bone destruction evident in temporal bone CT scans and necrotizing granulomatous inflammation in mastoid specimens [39]. Delayed diagnosis and treatment exacerbate bone destruction and hearing impairment. Radiological and surgical findings indicative of tuberculous mastoiditis warrant urgent tissue sampling from the middle ear cavity for microscopic, PCR (polymerase chain reaction), and histological examination, potentially obviating the need for further mastoidectomy. In tuberculosis-endemic regions, children displaying typical signs and necrotizing granulomatous inflammation should be promptly considered for antituberculosis therapy initiation until definitive diagnosis via GeneXpert PCR, Ziehl-Neelson staining, or positive Mycobacterium tuberculosis culture is confirmed.

Modern treatment methods

Cholesteatoma treatment is primarily surgical with microscope using, with two conventional methods: canal wall up (CWU) and canal wall down (CWD). The CWU technique involves exposing the mastoid and middle ear while preserving the bony structure of the external auditory canal. In contrast, the CWD approach involves removing the ear canal up to the vertical facial ridge and the bone covering the facial nerve, resulting in an open mastoid bowl that necessitates regular debridement in a clinical or surgical setting and long-term water precautions. [40] In the pediatric population, the CWU technique provides better long-term post-operative care and facilitates improved hearing rehabilitation. However, a systematic review encompassing both children and adults found no significant differences in recurrence rates or residual disease between the techniques. However, the limited visibility offered by the microscope makes it challenging to detect lesions concealed in the anterior epitympanic recess and tympanic sinus, potentially resulting in residual lesions and cholesteatoma recurrence [41]. Apart from surgical resection, the emergence of endoscopic technologies has brought attention to transcanal endoscopic ear surgery as a treatment option for cholesteatoma, particularly in pediatric cases [42]. Utilizing angled endoscopes (30 and 45°), transcanal endoscopic ear surgery enables clear visualization of concealed areas like the retrotympanum, anterior epitypanum, facial recess, and sinus tympanum [43-44]. This minimally invasive approach employs a transcanal method, avoiding retroauricular incisions [45].

Meta-analysis of 13 studies made by Bo Li et al. showed that endoscopic ear surgery (EES) offered notable advantages for patients with middle ear cholesteatoma. Those who underwent EES had fewer residual lesions and lower recurrence rates compared to those who received conventional microscopic ear surgery (MES). However, there were no significant differences in operation times or other postoperative outcomes, such as graft success rates and auditory performance, between EES and MES. Additional high-quality prospective studies are needed to further validate the benefits of endoscopic techniques in

middle ear cholesteatoma surgery [46]. However, despite its potential benefits, transcanal endoscopic ear surgery has not seen widespread adoption in practice due to limitations such as single-handed maneuverability, depth perception challenges, difficulty in ossicular reconstruction, endoscope tip fogging, and the risk of facial nerve and chorda tympani damage [47].

Laser usage has become prevalent in cholesteatoma treatment over the past two decades, particularly in the United States. The potassium titanyl phosphate laser, operating at a wavelength of 532 nm, is commonly employed. Laser application enables atraumatic removal of middle ear cholesteatoma and the ossicular chain, along with precise hemostatic removal of affected tissues such as polyps, granulations, and adhesions [48]. Retrospective studies indicate a halved risk of residual cholesteatoma with laser treatment.

Conclusion

The review pays special attention to publications devoted to current trends in radiological diagnosis of temporal bone pathologies. In modern practice, clinicians try to give preference to non-ionizing research methods. Indications for using magnetic resonance imaging of the temporal bones are constantly expanding, and techniques for merging data with computed tomography data are being introduced. In treating complicated diseases in foreign practice, more gentle modern endoscopic and laser correction methods are also used, which help reduce the risk of recurrence and postoperative complications.

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The Effect of Supine, Semi-Fowler's, and Fowler's Positions on the Blood Pressure Values of Patients Hospitalized in Surgical Clinics

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Abstract

Aim: Blood pressure measurement is an integral part of clinical practice in patient care and treatment, as well as being of critical importance in the early diagnosis, treatment, and prevention of the complications of hypertension. This study was carried out to determine the effect of Supine, Semi-Fowler's, and Fowler's positions on the blood pressure values of patients hospitalized in surgical clinics.

Material and methods: This quasi-experimental study was carried out with 112 preoperative surgical patients hospitalized in the surgical clinics of a training and research hospital. Using a bedside monitor, the patients' systolic and diastolic blood pressures were measured in the supine, Fowler's, and semi-Fowler's positions. The Pearson correlation coefficient, Mauchly's sphericity, ANOVA, and Bonferroni correction were used in the data analysis.

Results: While systolic blood pressure values did not differ between the Supine and Semi-Fowler's positions (F = .007, p = .934), there was a significant difference between the Semi-Fowler's and Fowler's positions (F =5.534, p = .020). Diastolic blood pressure values differed significantly between the Supine and Semi-Fowler's (F = 7.406, p = .008) and Semi-Fowler's and Fowler's (F = 9.038, p = .003) positions.

Conclusions: It is vital for nurses to establish procedures for blood pressure measurement and evaluation in the clinic and other team members and periodically revise the existing procedures.

Keywords: diastolic pressure, systolic pressure, posture, nursing, preoperative procedure.

Introduction

Blood pressure (BP) measurement is an integral part of clinical practice in patient care and treatment. It is of critical importance in the early diagnosis, treatment, and prevention of the complications of hypertension [1]. The BP measurement is one of the most frequently used applications in interventional studies, public health research, and clinical examination and treatment [2]. The accuracy of BP measurement plays a vital role in preventing hypertension and reducing morbidity, which is a significant public health problem [3]. The prevalence of hypertension, which was seen in 1.13 billion people in Central and Eastern Europe in 2015, is 30-45%. It is estimated that this rate will increase by 15-20% by 2025 and reach 1.5 billion [4]. In Turkey, the prevalence of hypertension in the adult age group is 33%, as reported by the Turkish Society of Cardiology [5].

Many factors such as environmental factors (environmental temperature, noise, etc.), patient-related conditions (position, measurement area, physical activity status, eating and drinking status, smoking, caffeine consumption, etc.), diseases related to the measurement device (sensitivity of the device, cuff size, calibration status, etc.), measurement time, knowledge of the person making the measurement, and white coat effect can affect the BP measurement value [6, 7]. In general, differences

in BP measurement results from 1-2 mmHg to 20-50 mmHg can be seen in individual applications. Observing such significant differences as a result of the measurement may have effects that will change the care and treatment options of the patient [2]. In a study conducted in Canada and England, a systolic BP (SBP) of 3-5 mmHg increases the number of people diagnosed with hypertension by 24% to 43% [8]. Low BP measurements cause a delay in diagnosis and treatment, and high readings cause misdiagnosis and the start of incorrect treatment and diet [3, 9]. At this point, it is important to use procedures in blood pressure measurement. Various guidelines have been published with the aim of improving the accuracy of BP measurements by standardizing relevant procedures. These guidelines address measurements taken primarily from the upper arm and generally include recommendations regarding patient posture, cuff size, arm height, cuff descent rate, and number of repeated measurements [10].

In two studies conducted with physicians, when blood pressure was high, physicians tended to order more tests and evaluated patients' emotional problems [11-12]. There is no mention of an approach to how and where the nurse measures blood pressure. This shows that procedures for measuring blood pressure are needed. Generally, measurement values obtained from the upper arm are used in blood pressure evaluation. Although this standard technique seems simple, many consecutive steps are required to obtain a reliable result. Nurses and doctors often deviate from this technique [13]. A 5 mmHg difference in systolic blood pressure causes misclassification of hypertension status in 84 million people worldwide [14]. The recommended sitting position with arm and back support is not always clinically possible for various conditions or conditions such as pregnancy. It has been determined that clinically significant differences in blood pressure values may occur depending on patient position [15]. Therefore, it is clinically important to understand the effects of alternative patient positioning on blood pressure measurements.

In the literature review, the results of the studies on whether there is a difference between the semi-Fowler's, Fowler's, and supine positions, which are frequently used for BP measurement in clinical practice, are limited. Therefore, the present study was carried out to determine the effect of supine, semi-Fowler's, and Fowler's positions on the BP values of patients hospitalized in surgical clinics.

Research Questions

The research questions in our study were as follows:

- Do the supine, semi-Fowler's, and Fowler's positions affect the BP values of patients hospitalized in surgical clinics?
- Is there a difference between the measured SBP/ diastolic BP (DBP) and the lowest and highest normal BP values?

Material and methods

Study Design and Sample

This quasi-experimental study was carried out with surgical patients. They were hospitalized in the surgical clinics of a training and research hospital in Turkey's Eastern Black Sea region. The study population comprised 112 patients who were hospitalized in surgical units, including general surgery, urology, orthopedics and traumatology, ophthalmology, and neurosurgery between January and August 2021. The study's sample size was determined as 112 by conducting power analysis and taking the effect power as 0.80 and the effect size as 0.60.

The inclusion criteria were as follows:

- having no diagnosis of hypertension,
- having no cardiovascular disease,
- having body mass index (BMI) not greater than 45, and
- volunteering to participate in the study.

The exclusion criteria were as follows:

- using non-steroidal anti-inflammatory drugs,
- having communication problems,
- pregnant, and
- having skin lesions or limitation of movement in the arm and leg from which measurements will be obtained.

Study Protocol and Data Collection

Patients hospitalized in surgical clinics and who met the sampling criteria were first informed about the study. Those who agreed to participate in the study signed an informed consent form. Age, sex, height, weight, BMI, heart rate, and saturation value without BP measurement were recorded in the patients who met the sampling criteria and agreed to participate. Due to the COVID-19 pandemic, the patients were wearing masks but removed those five minutes before the oxygen saturation measurement, because a mask can affect the patients' saturation values, and then the values were measured. The research data were collected and recorded during the preoperative period. Some patients may have had limited mobility during the postoperative period, and positioning was difficult or contraindicated (hip and knee prosthesis operation, lumbar disc hernia, etc.). A calibrated and noninvasive bedside monitor was used for all BP measurements. A bedside monitor was chosen to avoid individual measurement differences and to use a standard device in the study. The bedside monitor was used to collect data only during the research implementation.

BP measurements as described in the 2018 Hypertension Management Guidelines of the European Society of Cardiology (ESC) were followed [4]. To determine the size of the cuff to be applied, arm circumference was measured, and the appropriate cuff was used for BP measurement (small <24, medium 24-34, large >34 cm). Before all measurements, the patients rested for at least 5 minutes. There was no conversation between the researcher and the patient during the measurement. There was no noise, and the room temperature was 21 °C. The patients wore loose comfortable clothes, and they did not cross their legs. If the patients had smoked or consumed food or any caffeinated drink before BP was due to be measured, the measurement was performed after waiting at least 30 minutes. BP values were obtained from both arms between 10 and 12 o'clock. If the difference between the measurements was more than 15 mmHg, the measurement was repeated. If there was more than a 15 mmHg difference between the two arms, the physician was told to evaluate the patient and not include him/her in the study sample. If the measurement difference was less than 15 mmHg, the higher measurement was recorded. First, measurements were made while the patient was in the supine position; then BP measurements were made by placing him/her in the semi-Fowler's and Fowler's positions. After the patient was moved into a different position and rested for 5 minutes, BP values were measured in the supine, semi-Fowler's, and Fowler's positions.

Supine Position: The patients had their legs extended straight, their arms at their sides, palms facing upwards, and their arms were supported by a pillow at heart level in the supine position. A cuff of appropriate size was placed on the brachial artery by palpation. SBP and DBP were measured in the supine

position in both arms. A third measurement was made and recorded if the difference was more than 5 mmHg between it and the previous ones. If the difference between the measurements was not more than 5 mmHg, the SBP and DBP in the higher BP arm were taken, and the mean BP value was calculated and recorded.

Semi-Fowler's Position: The patient's head was raised 45°, the back was supported by a pillow, and the legs were extended straight. The arms at heart level were supported by a pillow underneath, with the palms facing upwards. A cuff of appropriate size was placed on the brachial artery by palpation. In the BP measurement, SBP and DBP were taken in both arms in the semi-Fowler's position. A third measurement was made and recorded when there was a difference of more than 5 mmHg between it and the previous ones.

Fowler's Position: The patient's head was raised 90°, the back was supported by a pillow, and the legs were extended straight. The arms at heart level were supported by a pillow underneath, with the palms facing upwards. A cuff of appropriate size was placed on the brachial artery by palpation. The SBP and DBP were measured in both arms in the Fowler's position. A third measurement was made and recorded when there was a difference of more than 5 mmHg between it and the previous ones. When there was no difference between the measurements, SBP and DBP in the higher BP arm were recorded.

Measurements/Instruments

A questionnaire, which consisted of a Patients' Sociodemographic Form and a Physical Assessment Form, was used to collect the data. In the Patients' Sociodemographic Form, there were questions related to age, sex, marital status, family structure, residence, educational level, department, history of smoking, and current smoking. The Physical Assessment Form included weight, height, BMI, heart rate, respiratory rate, oxygen saturation, position, SBP, DBP, and arm circumference.

Ethical Considerations

The principles of the Declaration of Helsinki were considered at all stages of the study. It was explained to the participants that their personal information would not be shared with anyone, their identities would be kept confidential, and they could withdraw from the research whenever they wanted. For the implementation of the study, permission was obtained from the University Ethics Committee (05.12.2019/18). Written and verbal consent was obtained from the patients who participated in the study.

Data Analysis

IBM SPSS Statistics 25.0 (IBM, Armonk, NY, USA) was used to analyze the research data. Descriptive statistics such as number, percentage, arithmetic mean, standard deviation, and minimum and maximum values were used to analyze the descriptive data. The reliability of the scales was evaluated with the Cronbach alpha coefficient. The Shapiro–Wilk W test was used to assess the compliance of BP measurements with a normal distribution ($p>0.05$). Pearson's correlation coefficient test was used for the relationship between the measurements since the data showed a normal distribution. The sphericity assumption was tested with Mauchly's sphericity test and met ($p>0.05$). ANOVA was used in repeated measurements to determine the difference between BP measurements according to positions. Bonferroni correction was used for pairwise comparisons. A one-sample t-test was used to determine whether the SBP and DBP values obtained due to the measurements differed from the normal BP values. The lowest and highest normal BP values were obtained from the ESC and the ESH [4]. P values < 0.05 were regarded as statistically significant.

Results

Participants Characteristics

The mean age of the patients was 48.91 ± 14.37 years, 54.5% were male, 84.8% were married, and 84.6% had a nuclear family structure. Moreover, 30.4% were primary school graduates and 36.6% were hospitalized in the general surgery service. Only 22.3% were smokers, while 43.8% were previous smokers. Of the participants, 44.6% were overweight (Table 1).

Physiological Findings and Blood Pressure Measurements

The mean heart rates of the patients were 75.89 ± 10.07, respiration rate was 18.03 ± 1.98, and oxygen saturation was 96.68 ± 1.66. The Fowler's position's mean SBP and DBP were 122.69 ± 12.27 and 75.89 ± 8.25, respectively. In the semi-Fowler's position, the mean SBP was 121.22 ± 12.31 and the mean DBP was 74.28 ± 8.87.

Table 1 Demographic characteristics of the patients

Variables	n	%
Age (mean ± SD)	48.91 ± 14.37	
Gender		
Female	51	45.5
Male	61	54.5
Marital status		
Married	95	84.8
Single	17	15.2
Family structure		
Nuclear	106	94.6
Extended	6	5.4
Place of residence		
Village	29	25.9
Town	36	32.1
City	47	42.0
Educational status		
Illiterate	23	20.5
Primary school	34	30.4
Secondary school	19	17.0
High school	29	25.9
University	7	6.3
Department		
General surgery	41	36.6
Urology	35	31.3
Orthopedics and traumatology	21	18.8
Eye disease	4	3.6
Neurosurgery	11	9.8
Smoking		
Yes	25	22.3
No	87	77.7
History of smoking		
Yes	49	43.8
No	63	56.3
Body Mass Index (BMI)		
≤18.49 (underweight)	2	1.8
18.50-24.99 (normal)	31	27.7
25.00- 29.99 (overweight)	50	44.6
≥30 (obese)	29	25.9

The mean arm circumference was 27.08 ± 2.83. Considering the BP values, the mean SBP and DBP in the supine position were 121.16 ± 11.63 and 72.93 ± 9.01, respectively (Table 2). Figure 1 shows SBP measurements. Figure 2 shows DBP measurements. Figure 3 shows mean BP measurements.

Table 2 Physiological findings and blood pressure measurements

Variables	Min.	Max.	Mean ± SD
Pulse	44.00	102.00	75.89 ± 10.07
Respiratory	12.00	24.00	18.03 ± 1.98
Oxygen saturation	90.00	99.00	96.68 ± 1.66
Supine systolic BP	89.00	143.00	121.16 ± 11.63
Supine diastolic BP	53.00	99.00	72.93 ± 9.01
Supine mean BP	66.00	113.00	88.50 ± 8.83
Semi-Fowler's systolic BP	90.00	145.00	121.22 ± 12.31
Semi-Fowler's diastolic BP	53.00	93.00	74.28 ± 8.87
Semi-Fowler's mean BP	68.00	108.00	89.45 ± 8.80
Fowler's systolic BP	95.00	148.00	122.69 ± 12.27
Fowler's diastolic BP	53.00	96.00	75.89 ± 8.25
Fowler's mean BP	72.00	110.00	91.15 ± 8.34
Arm circumference	19.00	35.00	27.08 ± 2.83

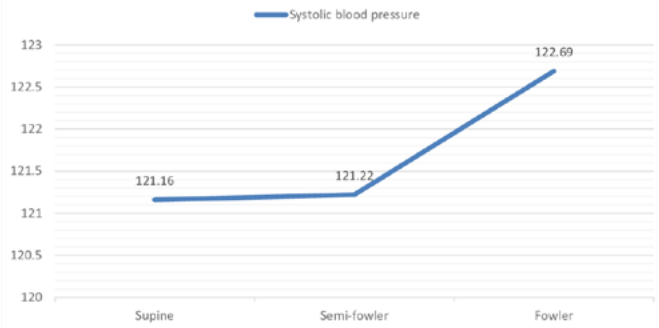

Figure 1 – Systolic blood pressure measurements

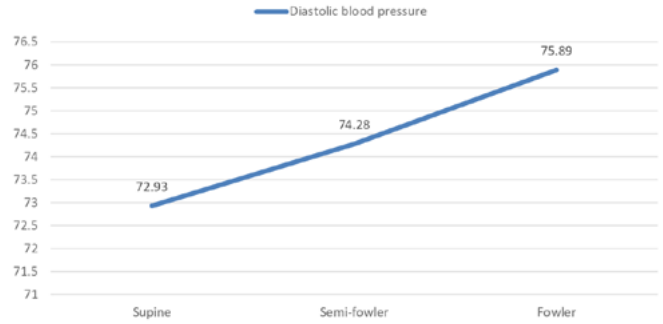

Figure 2 – Diastolic blood pressure measurements

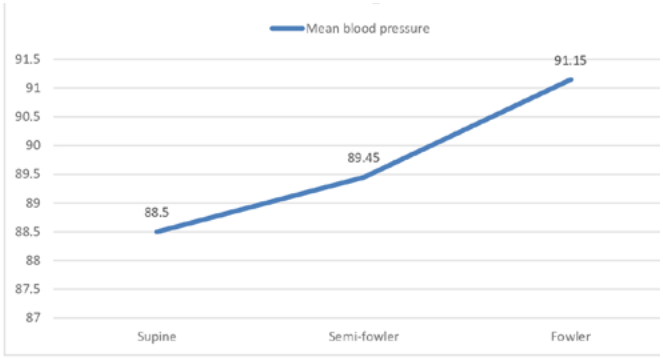

Figure 3 – Mean blood pressure measurements

Correlation Findings

Table 3 shows the correlation findings between the measurements. There was a positive and strong correlation between BP measurements in the supine position and those in the semi-Fowler's (r = 0.853) and Fowler's (r = 0.815) positions ($p < 0.05$). There was also a statistically significant strong correlation between BP measurements in the semi-Fowler's and Fowler's positions (r = 0.824, $p < 0.05$).

Blood Pressure Measurements According to Positions

There was a statistically significant difference between patients' SBP (F = 3.621, p = 0.028), DBP (F = 14.889, p < 0.001), and mean BP (F = 15.814, p < 0.001) measurements according to one-way ANOVA with repeated measures (Table 4).

Table 3 Pearson correlation coefficient between blood pressure measurements

Variables	1	2	3	4	5	6	7	8	9
Supine systolic BP (1)	1								
Supine diastolic BP (2)	00.621*	1							
Supine mean BP (3)	00.853*	0.914*	1						
Semi-Fowler's systolic BP (4)	00.839*	0.531*	0.740*	1					
Semi-Fowler's diastolic BP (5)	0.560*	0.828*	0.788*	0.607*	1				
Semi-Fowler's mean BP (6)	0.745*	0.789*	0.853*	0.829*	0.879*	1			
Fowler's systolic BP (7)	0.831*	0.489*	0.709*	0.855*	0.533*	0.724*	1		
Fowler's diastolic BP (8)	0.555*	0.740*	0.740*	0.571*	0.784*	0.726*	0.631*	1	
Fowler's mean BP (9)	0.748*	0.711*	0.815*	0.766*	0.745*	0.824*	0.863*	0.908*	1

Table 4 Comparison of blood pressure measurements according to positions

Position	Mean systolic BP	Mean diastolic BP	Mean BP
Supine position	121.16 ±11.63	72.93 ± 9.01	88.50 ± 8.83
Semi-Fowler's position	121.22 ± 12.31	74.28 ± 8.87	89.45 ± 8.80
Fowler's position	122.69 ± 12.27	75.89 ± 8.25	91.15 ± 8.34
F	3.621	14.889	15.814
p	0.028	0.000	0.000

While SBP values did not differ between the supine and semi-Fowler's positions (F = 0.007, p = 0.934), there was a significant difference between the semi-Fowler's and Fowler's positions (F =5.534, p = 0.020). DBP values differed significantly between the supine and semi-Fowler's (F = 7.406, p = 0.008) and semi-Fowler's and Fowler's (F = 9.038, p = 0.003) positions (Table 5).

Table 5 Pairwise comparisons according to Bonferroni correction

Blood pressure	Position	F	p
Systolic BP	Supine vs. Semi-Fowler's	0.007	0.934
	Semi-Fowler's vs. Fowler's	5.534	0.020
Diastolic BP	Supine vs. Semi-Fowler's	7.406	0.008
	Semi-Fowler's vs. Fowler's	9.038	0.003
Mean BP	Supine vs. Semi-Fowler's	4.459	0.037
	Semi-Fowler's vs. Fowler's	12.338	0.001

Table 6 Comparison of the mean systolic and diastolic BP measured with the lowest and highest normal BP values

Position	Systolic blood pressure				
	Reference systolic blood pressure value	Measured systolic BP value	Mean difference	t	p
Supine systolic BP (1)	1				
Supine diastolic BP (2)	00.621*	1			
Supine mean BP (3)	00.853*	0.914*	1		
Semi-Fowler's systolic BP (4)	00.839*	0.531*	0.740*	1	
Semi-Fowler's diastolic BP (5)	0.560*	0.828*	0.788*	0.607*	1
Semi-Fowler's mean BP (6)	0.745*	0.789*	0.853*	0.829*	0.879*
Fowler's systolic BP (7)	0.831*	0.489*	0.709*	0.855*	0.533*
Fowler's diastolic BP (8)	0.555*	0.740*	0.740*	0.571*	0.784*
Fowler's mean BP (9)	0.748*	0.711*	0.815*	0.766*	0.745*

In Table 6, the mean SBP and DBP measured with normal BP values are compared. There was no significant difference between the normal SBP value and the supine and semi-Fowler's SBP values ($p = 0.290$, $p = 0.295$, respectively). In addition, although the SBP value in the Fowler's position was significantly higher than the normal value ($p = 0.022$), it was lower than the highest value considered normal ($p < 0.001$). There was a statistically significant difference between normal DBP and supine, semi-Fowler's, and Fowler's BP values ($p < 0.001$).

Discussion

In our study, the SBP value in the supine position was lower than the values in the semi-Fowler's and Fowler's positions. The SBP value was highest in the Fowler's position. According to the ESC and ESH, the optimal BP value is <120 mmHg for SPB [4]. While there was no difference between this value and the average of the measurements made in the supine and semi-Fowler's positions, the value obtained in the Fowler's position was higher than the optimal value. According to the ESC and ESH, the highest SBP value considered normal is 129 mmHg [4]. Based on this value, the average of the measurements in the supine, semi-Fowler's, and Fowler's positions was low. The reference value for a normal systolic blood pressure is 120 mmHg [16]. They stated that BP might vary according to whether the patient is lying down, sitting, or standing. In this case, the SBP values measured according to the positions (120-129 mmHg) were accepted as normal by the ESC and ESR [4]. However, a 120-129 mmHg SBP is considered a risk for high BP and hypertension [17, 18]. Therefore, choosing the position with the lowest SBP in the measurement may be essential along with always using the same position.

In the present study, when the DBP measurements in the three different positions were compared, DBP was lowest in the supine position and highest in the Fowler's position. The lowest and highest DBP values that are considered normal according to the ESC and ESR are 80-84 mmHg [4]. DBP values obtained in the supine, semi-Fowler's, and Fowler's positions in the present study were low compared to both values considered normal. Other vital signs of the patients were in the normal range, and it can be concluded that the patient's condition is stable. In this case, the normal DBP value may need to be reconsidered for hospitalized patients, because an increase in DBP above 10 mmHg doubles the risk of death from cardiovascular disease [19]. Therefore, it may be beneficial for nurses to review BP values and establish BP measurement and evaluation procedures.

In the present study, the SBP and DBP values generally differed according to the positions, and the values in the Fowler's position were higher than those in the other positions. Similar to our study, Myers et al. [15] found that SBP, DBP, and mean BP values were lower in the supine position compared to in the Fowler's position. However, Eşer et al. [20] found that SBP showed a significant difference according to position, while DBP values did not change. The SBP in the supine position was higher than that in the other positions. In a study comparing brachial and aortic BP values according to sitting and supine positions, SBP was more increased in the supine position, while DBP was higher in the sitting position [21]. In another study, while there was no difference in patients' systolic blood pressure values according to the Semi-Fowler position, there was a significant increase in the Supine position [22]. Like the present study, Privsek et al. [23] found that both SBP and DBP values in the sitting position were higher than those in the supine position. As can be seen, the study findings differ. Based on the results of our study, the position given to the patient during BP measurement is important. In addition, measuring BP in the same position during the treatment and care of the patient may prevent differences that may occur in the measurement results and the wrong treatment and interventions applied accordingly.

BP measurements are affected by physiological factors such as the patient's emotional state, body temperature, respiration rate, bladder distension, pain, exercise, age, food consumption, tobacco and alcohol use, and medical conditions [24]. One study compared doctors, nurses, and nurse assistants and found that knowledge of accurate blood pressure measurement was higher in doctors [25]. Freire et al. [26] found that factors affecting BP values are adiposity, glycemia, smoking, physical activity, alcohol consumption, and socioeconomic status. These factors make it difficult to measure BP accurately. However, it can be beneficial to identify and control controllable factors such as exercise, food, and position. In the present study, factors such as measuring instrument, cuff size, speech, noise, temperature, position, clothing, food, smoking, tea, caffeinated food, and measurement techniques were kept under control during the measurement.

Limitations of the Study

The study has some limitations. It was conducted in a single center. Therefore, it cannot be generalized to the whole universe. Future studies may be undertaken in larger samples and more than one center. Measurements were automatically measured using a bedside monitor. Comparative studies on manual and automatic measurement can be conducted.

Conclusion

In the present study, the supine, semi-Fowler's, and Fowler's positions that hospitalized patients were placed in significantly affected SBP and DBP measurements, and the measurement values were different. BP measurements should always be made in the same position during the hospitalization of patients for an accurate evaluation. More studies are needed on the effect of positions on BP and the reference range in which BP values will be evaluated. It is vital for nurses to establish procedures for BP measurement and evaluation in the clinic and other team members and revise the existing procedures periodically. In addition, since two or more measurement methods are not routinely performed in clinical practice, it is essential to inform nurses about the measurement strategy and emphasize this issue in training. Meticulous evaluation and control of the factors affecting BP will also contribute to accurate BP measurement.

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Cardiac Surgery Associated Acute Kidney Injury, Incidence, and Predictors. Prospective Observational Single Center Study

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Abstract

Acute kidney injury (AKI) is a condition characterized by a sudden decline in kidney function, leading to accumulation of waste products and fluids in the body. It is a common and serious complication in patients with cardiovascular diseases, and it is associated with increased morbidity and mortality.

Aim: In this study, we explore the relationship between cardiac issues and the development of AKI, as well as strategies for its prevention and management. The primary aim of this study is to examine the incidence and risk factors for the AKI in patients admitted to the cardiac intensive care unit/ CICU), as well as the impact of AKI on patient outcomes.

Methods: We conducted prospective observational single center study. 292 consecutive patients admitted to ICU after open heart surgery by sternotomy were included. Patients were monitored in ICU for frequency of AKI, perioperative risk factors, cardiac surgery-associated acute kidney injury (CSA-AKI) and their impact on patients' outcome.

Results: After admission to the intensive care unit, 33 patients (11.3%) developed CSA-AKI in the postoperative period. According to the analysis, male gender (p=0.03), decreased GFR (p=0.02) as well as high EuroSCORE II (p=0.013), hemoglobin level before surgery (p = 0.002) and the presence of diabetes and chronic kidney disease (p=0.03) were independent predictors of AKI after open-heart surgery. In patients who developed AKI, the duration of artificial lung ventilation was increased (21.3 vs 9.9 hours p = 0.001) and the duration of stay in the intensive care unit (4.3 vs. 1.9 days, P = 0.02).

Conclusion: Patients often have AKI after heart surgery. EuroSCORE II, gender, diabetes, time of cardiopulmonary bypass and chronic kidney disease are independent predictors of AKI development. The appearance of AKI is due to an unfavorable outcome of events. The appearance of acute kidney injury is associated with adverse consequences.

Keywords: acute kidney injury, cardiac surgery, predictors of AKI, postoperative period, complications.

Introduction

Kidney injuries that occur following heart surgeries are referred as cardiac surgery associated acute kidney injuries (CSA-AKI) [1]. AKI is a frequent sequela after heart surgery, with the incidence reaching up to 30% and potentially serious negative consequences for a patient [2].

Understanding the risk factors and subsequent early CSA-AKI management is crucial for improving patient care and reducing the burden of this complication.

In this document, we will explore the etiology, clinical implications, diagnostic criteria, and management strategies for CSA-AKI. By gaining deeper understanding of this condition, healthcare providers can work towards implementing evidence-based practices to mitigate the risk and impact of CSA-AKI [3, 4].

CSA-AKI is a common complication among cardiac surgery patients, leading to longer ICU stays [5]. Despite advancements in surgical methodologies and perioperative care, postoperative incidence of AKI remains relatively high. CSA-AKI is a multifactorial condition that involves a complex interplay of patient comorbidities, perioperative factors, and postoperative management [6]. The etiology of AKI in this setting is often linked to the use of cardiopulmonary bypass, ischemia-reperfusion injury, and exposure to nephrotoxic agents [2]. Understanding these underlying mechanisms is paramount to develop effective preventive strategies and optimize patient care. CSA-AKI slows down cardiac surgery patients' recovery in up to 30% of cases [7].

In addition to the immediate clinical implications, CSA-AKI is linked to increased probability of occurrence of chronic kidney disease (CKD), cardiovascular events, and mortality. Addressing the diagnostic challenges and implementing timely management interventions is essential to minimize the impact of AKI on patient morbidity and mortality [3, 8]. Therefore, it is crucial for healthcare providers to have a comprehensive understanding of the risk factors, pathophysiology, diagnostic criteria, and management strategies for cardiac surgery patients [9].

Current work targets to study the prevalence of CSA-AKI in the immediate setting and to assess the perioperative risk factors for CSA-AKI after heart surgery and their association with subsequent morbidities and mortalities.

Material and methods

During a prospective observational study, data was gathered from patients in the ICU department at the National Research Cardiac Surgery Center from October 2023 to January 2024. All included patients received treatment based on the standard of care protocol. Consent for conducting the study was received from the local bioethics panel of NRCSC (N 01-74/2021 dated 10/06/20).

ICU patients older than 18 years who have undergone open heart surgery and were diagnosed with AKI in the postoperative period (within 48 hours, according to "Kidney disease: Improving global outcomes" criteria) were included in the investigation. The participants with the previously present end-stage renal failure undergoing dialysis were excluded from the study.

All consecutive patients who were admitted to the ICU after undergoing open heart surgery via sternotomy were enrolled in the investigation. The patients were followed to define the incidence of AKI, possible postoperative risks for CSA-AKI, as well as their impact on outcomes in the ICU.

Demographic data and the initial clinical preoperative parameters of the patients are shown in Table 1. CKD was determined based on the presence of an estimated glomerular filtration rate (eGFR) lower than 60 ml/min/1.73 m^2 as calculated using the CKD-EPI formulation.

The study observed the length of mechanical ventilation, the length of stay in the ICU, frailty, delirium, re-intubation, dialysis, and ICU mortality. The initial outcome was to estimate the incidence of CSA-AKI. Secondary objectives included

Table 1 Demographic data and the initial clinical preoperative parameters of the patients

Total population (%)	N(%)	AKI	No AKI	P value
	292	33(11.3%)	259 (88.7%)	
Baseline pre-operative characteristics				
Gender, female	90 (30.82)	10 (30.3%)	80 (30.9)	0.54
Gender, male	202 (69.2)	23 (69.7%)	179 (69.1)	0.03
Age (year)	62.8 (22-79)	69 (31–74)	65.1 (21–79)	0.57
BMI (kg/m2)	26.7 (23.1 32.6)	27.64 (25.6-30.5)	27.68 (22.5-30.7)	0.62
EuroScore II (%)	1.7 (1.09-2.9)	2.54 (1.52–4.4)	1.5 (0.94–2.4)	0.03
Hb (gr/dL)	13.9 (9.6-15)	11.4 (7.6–12.3)	12.2 (9.5–14.0)	0.23
WBC (×103/μL)	10.3(7.9-13.1)	11.4 (8.9–13.7)	10.5 (7.5–12.8)	0.63
Creatinine (mg/dL)	1.03 (0.8-1.4)	1.19 (0.9–1.4)	0.9 (0.8–1.1)	0.12
eGFR (mL/min/1.73 m2)	79.1 (60.2-89.9)	59.3 (52.3-84.2)	81.3 (63.1-90.8)	0.02
concomitant diseases				
hypertension	165(65.5)	27(16.36)	138(83.64)	0.04
CKD	50 (17.12)	22 (44%)	28 (56%)	0.04
diabetes type II	155(53.1)	23(14.83)	132(85.16)	0.03
ischemic Stroke	26(8.9)	12(46.15)	14(53.85)	0.27
Intraoperative characteristics				
Duration of CPB (min)	123 (80-184)	137 (112–184)	101 (80–132)	0.01
Aortic cross-clamp time (min)	81 (56-125)	93 (59–125)	69 (56–104)	0.02
Structure of surgeries				
CABG	167	7	160	0.63
Heart valve repair	**82**	**13**	**69**	**0.67**
Aortic valve replacement	20	5	15	0.74
Mitral valve replacement	18	2	16	0.21
Tricuspid valve replacement	17	2	15	0.3
Mixed valve replacement	27	4	23	0.07
LVAD	14	4	10	0.12
Bentall de Bono	15	3	12	0.63
Aortic arch debranshing	3	2	1	0.55
Supracoronary aortic arch replacement	8	2	6	0.17
Heart transplant	3	2	1	
Post-operative characteristics				
Duration of mechanical ventilation (hours)	12.5±3.5	21.3±6.43	9.9±5.15	0.001
LOS ICU days	2.69±3.15	4.3 ±3.6	1.9 ±2.9	0.02
Re-intubation, n (%)	11	9.00	2	0.027
Fluid balance 24 h post-surgery (mL)	712±154	1563±582	312± 205	0.001
VIS max	5.14±3.12	16.27±3.9	6.6±3.1	0.022
Mortality rate	14 (4.79%)	8 (57.15%)	6 (42.85%)	

AKI: Acute kidney injury; BMI: Body mass index, Hb: Hemoglobin, WBC: White blood cells; sCr: Serum creatinine, HTN: Hypertension; CKD: Chronic kidney disease defined as eGFR ≤ 60 mL/min/173m2; PAD: Peripheral artery disease; CPB: Cardiopulmonary bypass, ICU: Intensive care unit. VIS – vasopressor inotropic score. All continuous variables are presented as median (interquartile range) and categorical variables as absolute values (%). Statistical significance was set at P value less than 0.05.

guidelines, Table 2. and The Cleveland Clinic Scale is best suited for the diagnosis of CK-AKI requiring dialysis (Table 3). Baseline serum creatinine was measured 72 hours before surgery and monitored for 48 hours in the ICU after surgery.

Statistics

Data analysis involved using IBM SPSS Statistics version 26 software and R statistical software. Data following gaussian pattern of distribution was interpreted as means and their standard deviations, while non-normal data was summarized using medians and interquartile ranges. Categorical variables were represented as absolute and relative frequencies. The methods used for data analysis included univariate and multiple logistic regression models to determine the association between AKI development and risk factors.

Table 2 Serum creatinine level and urine output

Stage	Serum creatinine level	Urine output
1	Increase of ≥0.3 mg/dl (≥26.5 µmol/l) within 48 h or increase of 1.5–1.9-fold over baseline within 7 days	< 0.5 ml/kg/h for 6 to 12 h
2	Increase of 2.0–2.9-fold over baseline	< 0.5 ml/kg/h for 12 h
3	Increase of 3.0-fold over baseline, increase of ≥4.0 mg/dl (≥353.6 µmol/l), initiation of renal replacement therapy, or a GFR decrease < 35 ml/min/ 1.73 m^2 for patients < 18	< 0.3 ml/kg/h for 24 h or anuria for 12 h

KDIGO: Kidney Disease Improving Global Outcomes; AKI: acute kidney injury; GFR: glomerular filtration rate.

Table 3 Risk factors assessment

Risk factor	Score
Sex	1
c heart failure	1
35%	1
rative use of an intra-aortic balloon rpulsor	2
	1

assessing perioperative AKI risk factors and their association with clinical outcomes.

In our work, we analyzed the frequency of AKI occurrence and identified risk factors associated with open heart surgery that could impact ICU management and outcomes. Our findings revealed that AKI is a frequent consequence following cardiac surgery. The EuroSCORE II score, presence of type 2 diabetes, prior CKD, and leukocyte level in blood samples were independent parameters for AKI occurrence. AKI was linked to adverse sequences including length of mechanical ventilation, LOS, frequency of hemodialysis, re-intubation, delirium, and mortality.

CSA-AKI diagnosis was performed in accordance with the "Kidney disease: Improving global outcomes" (KDIGO)

Results

Clinical characteristics

Our study involved 292 patients, with a higher proportion being male (66.4%). According to KDIGO, 12.25% of the patients developed postoperative AKI. The demographic and clinical perioperative data for all patients are presented in Table 1. We performed various types of open-heart surgeries during the study, including heart transplants. Patients who acquired AKI were generally older and had a higher incidence of CKD, elevated values of EuroSCORE II. They also exhibited lower diastolic and mean blood pressure, along with an increased need for vasopressors and inotropes upon admission to the ICU compared to patients without AKI. Additionally, the patients with AKI had longer extracorporeal circulation and cross-clamping times during surgery, as well as an extended duration of general anesthesia and sedatives in the ICU, compared to patients without AKI.

The study revealed that certain parameters were linked to the development of CSA-AKI. These risk factors comprised a high EuroSCORE II value and a history of CKD.

The statistical analysis identified several significant predictors of AKI in the preoperative period. This included gender, with a male prevalence of 69.7% (p value = 0.03), a high EuroSCORE II value (95% CI: 2.54 vs 1.5, p = 0.003), GFR levels before surgery (95% CI: 59.1 vs 81.3, p = 0.02) and a history of CKD with an incidence rate of 66 % (p = 0.04) before surgery. Additionally, non-compensated arterial hypertension (p = 0.04) and type II diabetes were found to be independent predictive parameters for AKI.

The multifactorial analysis identified as well intraoperative parameters that may predict CSA-AKI, such as the duration of cardiopulmonary bypass (CPB) time (137 vs 101 minutes; p=0.01) and cross-clamp time (93 vs 69 minutes; p = 0.02).

AKI also has a negative impact on postoperative recovery in the ICU. Patients with AKI experienced significantly longer LOS in the ICU compared to those without AKI (4.3 vs 1.9 days, p = 0.02). There were also higher incidents of reintubation among patients with AKI and a substantial fluid retention leading to more than 1500 ml over 24 hours in the ICU (p = 0.001). The use of vasopressors and inotropic drugs, particularly when VIS max score was above 16 on the first day, showed a prominent association with the occurrence of AKI and adverse clinical outcomes such as prolonged mechanical ventilation, dialysis needs, and increased mortality rates for these patients.

AKI following cardiac surgery is associated with several negative clinical outcomes. These include longer durations of mechanical ventilation and higher LOS in the ICU, repeated intubation, and the need for dialysis.

Discussion

In our study, we found an increased occurrence of AKI in patients who had heart surgery. Our major results revealed that the severity score of the preoperative assessment, CKD, and diabetes were independent parameters of AKI development. Additionally, CSA-AKI incidence was strongly linked to unfavorable outcomes. Patients who developed post-surgery AKI experienced longer mechanical ventilation and intensive

care unit stays, higher rates of repeated intubation, dialysis requirement and mortality. These findings emphasize the importance of identifying high-risk patients and implementing strategies to prevent or mitigate the occurrence of AKI during postoperative period after cardiac procedure [2].

Current work results align with previous reports that have shown a moderate to high degree of AKI occurrence, as indicated by various definitions. Over time, numerous definitions were implemented to recognize and grade AKI disease. The criteria for classifying risk, injury, insufficiency, loss, and end-stage kidney disease were implemented in 2004; few years later there was a revision proposed by the Acute Kidney Injury Network group; finally, at the KDIGO workshop in 2012 a conjunction of RIFLE and AKIN suggestions were proposed.

The overall occurrence extent of AKI during postsurgical period comprised around 22.3%, determined applying RIFLE, AKIN or KDIGO definitions which shows similarity with our findings based on KDIGO criteria. Notably, studies using different criteria showed variations in the reported incidence rates - studies using KDIGO reported an incidence rate of 24.2%, while those using RIFLE or AKIN reported rates of approximately 18.9% and 28% respectively [10, 11].

Prolonged CPB duration, longer sedation therapy, and mechanical ventilation emerged as the primary intraoperative risk factors for CSA-AKI. Our study confirmed these associations through one-dimensional analysis but not with multivariate analysis. The mechanisms by which CPB launches AKI is comprehensive and not fully researched, including non-pulsating perfusion leading to renal ischemia [12], inflammation from CPB pump as well as the circuit resulting in free radicals assembly with consequent complement activation [13], as well as intravascular hemolysis causing damage to the renal tubules [14]. The link between extended CPB duration and the occurrence of CSA-AKI highlights the importance of optimizing intraoperative practices to reduce the incidence of this complication [2]. Optimizing intraoperative practices, such as minimizing CPB duration, sedation therapy, and mechanical ventilation, is crucial for reducing the risk of developing CSA-AKI in postoperative period.

Future works are required to fully decipher the pathophysiological scenario involved and to validate the potential biomarkers for routine use in different patient populations undergoing heart surgery [15].

In our work, we observed a tendency for an association between CSA-AKI and CPB length, as demonstrated by prior studies. A recent meta-analysis involving 2,157 patients during cardiac postoperative period, indicated that a higher CPB length is linked to a higher risk of developing CSA-AKI [16].

Conclusion

In conclusion, patients who have undergone open-heart surgery often experience postoperative CSA-AKI. EuroSCORE II, male gender, a history of diabetes, and CPB time are identified as independent risk factors for AKI occurrence in the postoperative period. Furthermore, the AKI incidence after surgery was found to be linked to the following negative outcomes such as extended mechanical ventilation, LOS, and higher rates of re-intubation.

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Correlation between Functionality and Quality of Life in Patients after Cardiac Surgery

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Abstract

Aim: Current research seeks to explore the correlation between early mobilisation in physical exercise and the functionality and life quality of patients post cardiac surgery.

Methods: A cohort of 100 patients, aged between 18 and 65, comprising 52 men and 48 women, participated in a program of early physical performance commencing from the first day through the seventh day post - heart surgery. Outcome measures included the 6 Minute-Walk Test (6MWT), the Short Form-International Physical Activity Questionaire (SF-IPAQ), and the Short Form-36 (SF-36). Each assessment was administered on the seventh day following cardiac surgery.

Results: Statistical analysis revealed a significant interrelation ($p<0.001$) with SFIPAQ SF-IPAQ scores and both the 6MWT and SF-36 scores. SF-IPAQ scores were inversely related to pain levels, they exhibited positive associations with energy-fatigue, social function, general health and functionality.

Conclusion: Our findings indicate that post - cardiac surgery patients exhibited improved degrees of physical performance, improved life quality, and enhanced functional ability.

Keywords: cardiac surgery, physical activity, life quality, correlation.

Introduction

Cardio-vascular diseases (CVD) comprise some conditions impacting the heart and vascular structures, containing coronary heart illness, cerebrovascular disorders, and congenital heart pathologies. Cardiovascular diseases account for roughly one-third of global mortality. Globally, CVD stands as the foremost cause of mortality and disability, with indications suggesting its enduring significance in the future [1].

Various issues, including endocarditis, rheumatic heart disease, and circulatory abnormalities, have the potential to impact the cardiovascular system [2]. Behavioral risk components related with cardiovascular disorder consist of, inactivity, smoking, intensive alcohol waste, diabetes, hypertension, elevated blood lipid levels, socioeconomic disadvantage, psychological stress, and genetic predisposition [3]. The primary treatment modalities for cardiovascular disease encompass pharmaceutical interventions, exercise regimens, dietary modifications, and surgical interventions [4].

Functional performance assessment, such as static balance tests or dynamic stability systems, is increasingly recognized as a valuable measure of outcomes in clinical research [5, 6]. It is commonly utilized for diagnosis, prognosis identification, comparison of patient responses to treatment, as well as for verifying and monitoring the guidance capacity performance, and development of therapies by therapists, and prevention of physical disabilities. Physical activity, recognized as a cornerstone health behavior, plays a primer role in the well-being of individuals with heart disease. Consistent and sufficient engagement in regular excercise enhances life quality and mitigates the likelihood of subsequent cardiovascular complications [7]. Diverse articles related postoperative physical activities have indicated that cases who engaged in cardiac rehabilitation or exercised under the guidance of a therapist post-cardiac surgery exhibited enhanced

cardiovascular capacity, reduced duration of hospitalization, and abbreviated overall length of stay [8]. Current studies reported that timely mobilization of patients post-operation should be regarded as a therapeutic approach within these patient cohorts [9, 10]. Nonetheless, contradictory outcomes from recent meta-analyses have revealed that among individuals undergoing cardiac surgery, early mobilization led to enhanced exercise tolerance [11]. However, in accordance with research conducted by Chen and colleagues, this intervention exhibited no impact on either the overall length of hospitalization or the duration in the intensive care service. [12]. This points the ongoing pertinence of studies in this research area [13, 14].

Nevertheless, despite the significance of early physical activity during the initial week following cardiac surgery, limited research has delved into the functional results and life quality, as well as the associated determinants, among patients during this crucial transitional phase [8, 11, 15]. Hence, the objective of current research was to evaluate the functional potential and life quality with cases that underwent cardiac surgery, while identifying factors associated with variations in functionality. Also current study aimed to evaluate evidence based exercise and early mobilization effectiveness on post cardiac surgeries physiological and psychological outcomes.

Material and methods

This prospective study contained patients who had undergone cardiac surgery. A total of 100 cases (52 male, 48 female) were recruited for the investigation. This research was conducted at Al-Bitar Cardiac Surgery Hospital, Baghdad, Iraq. This study approved by the regional ethics commission (897/2023/12/12), and all procedures were managed in according the standards delineated in the Declaration of Helsinki. Inclusion criteria were (1) undergone coronary artery bypass grafting, (2) successfully completed a six minute walk test, (3) aged 18 to 65. Patients were excluded if they had (1) an old cerebrovascular accidents, as others who had mental problems, (2) aged under 18 or over 65, (3) couldn't fill out surveys or do the six-minute walk test.

Interventions

During postoperative days 1 to 2, patients received shoulder-neck mobilization alongside breathing exercises and postural drainage. Subsequently, from postoperative days 3 to 7, the regimen comprised breathing exercises, postural drainage, and supervised walking sessions. The walking sessions involved gradual increments of 2.5 minutes, based on individual tolerance, up to ten minutes (three times per day).

Outcome measurements

All patients who participated in the surgical procedure on the 7th day underwent the administration of the following surveys, assessments, and examinations. The SF-IPAQ was employed to assess the grade of physical performance. The SF-36 questionnaire was utilized to evaluate life quality. Additionally, the 6MWT was conducted to gauge functional capacity.

36-Item Short Form

The SF-36 questionnaire comprises 36 questions derived from 21 components. Each item is allocated a score, that is subsequently ranging from 0 to 100 [16].

Short Form International Physical Activity Questionnaire

SF-IPAQ required participants to report the clinical characteristics of active moderate, and walking functions they engaged in the seven days past. They were put in place to give every activity an indicated metabolic equivalent of task (MET). Participants were categorized into high, moderate, and low physical activity stages based on their SF-IPAQ scores [17].

Six-Minute Walking Test

This test is a universally used, safe, and accepted assessment that may be used to evaluate participants' functional capacity in a range of the medical contexts. For the 6MWT, techniques that are endorsed by the American Thoracic Society were implemented. For this objective, a 30-meter-wide, obstruction-free channel was employed. The evaluation consists of instructing participants to cover a maximum distance of 6 minutes on foot. The greatest distance walked demonstrates a person's ability to move [18].

Sample size assessment

The sample size was determined by a Statistical Software (MediCalc,Belgium). The minimal requisited sample size was determined as 91 cases, guided by a power of 80% and the sample size was subsequently rised to 100 to account for any potential drop outs [19].

Statistical Analysis

Statistical analysis was carried out by SPSS-26 (IBM Co. USA). Numeric data were stated as a mean and standard deviation and analysed with two time points handling the Paired t-test. Pearson's correlation factor was computed to determine the impact of correlation. Linear regression test was employed to evaluate various independent items related with SF-IPAQ scores. A p-value of less than 0.05 was considered statistically significant.

Results

In this research, 100 cases withstanding cardiac surgery were enrolled, with 54%, 38% and 9% of them undergoing Coronary Artery By-pass Graft (CABG), valve replacement, and Atrial Septal Defect (ASD) surgeries, respectively. Male patients slightly outnumbered females, comprising 52% of the sample. The age range was 18 to 67, with a median of 53.15 ± 12.29 years, and the BMI varied from 16 to 46.40 kg/m^2, with a median of 26.81 ± 5.59 kg/m^2 (Table 1).

Table 1 Base level characteristics of the cases

Variables		N	%
Sex	Males	52	52
	Females	48	48
Age (years)	Mean ± SD	53.15 ± 12.29	
BMI (kg/m^2)	Mean ± SD	26.82 ± 5.58	
Marital status	Single	8	8
	Married	92	92
Education	Primary	62	62
	Secondary	8	8
	College	30	30
Smoking status		28	28
Drinking status		9	9
HTN level		58	58
DM level		41	41
Hyperlipidemia		59	59
Other diseases		19	19
Type of cardiac surgery	ASD	9	9
	Valve replacement	38	38
	CABG	54	54
Stay time in ICU	Mean ± SD	2.04 ± 0.2	
Surgical history		54	54

BMI: Body mass index, HTN: Hypertension, DM: Diabetes mellitus, ASD: Atrial septal defect, N: Number of patients, ICU: Intensive Care Unit (days), SD: Standard deviation.

There was a significant correlation found with SF-IPAQ scores and walking days per week (r=0.405, p<0.001) and walking duration (r=0.969, p<0.001). In addition, SF-IPAQ score was statistically significant reverse interrelated with age (r=-0.336, p=0.001) and Body mass index (r=-0.248, p=0.013), (Table 2).

There existed a statistically significant positive correlation found with SF-IPAQ scores and both the number of walking days per week (r=0.405, p<0.001) and the duration of walking in minutes (r=0.969, p<0.001). Conversely, SF-IPAQ scores exhibited a significant negative correlation with both age (r=-0.336, p=0.001) and BMI (r=-0.248, p=0.013), (Table 2).

Table 2 Correlation with SFIPAQ and characteristics of the cases

Variables	SF-IPAQ	
	r	P value
Age(years)	-0.336	0.001
BMI(kg/m^2)	-0.248	0.013
Stay duration in ICU (days)	0.014	0.888
Walking (days)	0.405	<0.001
Walking time (min)	0.969	<0.001

r: Pearson's coefficient, Statistical significance at P vale<0.005

In the 6MWT, the SF-IPAQ score demonstrated a significant positive correlation with peripheral oxygen saturation (SpO2), (r=0.247, p=0.013) and a negative correlation with mean arterial pressure, (r=-0.236, p=0.018). Additionally, a meaningful relationship was observed between the SF-IPAQ scores and the distance covered during the Six-minute walk (r=0.839, p<0.001), (Table 3).

Table 3 Correlation with SF-IPAQ and 6MWT scores

Variables	SF-IPAQ	
	r	p
Before 6 MWT		
SpO2 (%)	0.247	0.013
PR(bpm)	0.082	0.42
MAP (mmHg)	-0.236	0.018
After6MWT		
SpO2 (%)	0.167	0.097
PR (bpm)	0.007	0.946
MAP (mmHg)	-0.161	0.109
Distance Walked in 6 min (m)	0.839	<0.001

r: Pearson's correlation coefficient, Statistical significance at p value<0.05

According to regression analysis, Six-minute walk exhibited a significant association with the SF-IPAQ score (p<0.001), increasing 2.1 (95%CI: 1.82 to 2.37) with every 1 unit rise in the SF-IPAQ score. Similarly, in multiple regression analysis, Six-minute walk demonstrated a significant association with the SF-IPAQ score, increasing with 2.12 (95% CI: 1.83 - 2.4) per one unit rise in the SF-IPAQ score (Table 4).

As indicated in Table 5, a significant correlation existed with the SF-IPAQ and all SF-36 scores. Specifically, positive interrelations were observed with functionality (r=0.804, p<0.001), energy-fatigue (r=0.771, p<0.001), emotional wellbeing (r=0.648, p<0.001), social function (r=0.49, p<0.001), general health (r=0.658, p<0.001), and health change (r=0.781, p<0.001), while a negative correlation was found with the pain scores (r=-0.799, p<0.01).

Table 4 Lineer regression analysis of SF-IPAQ and 6-MWT scores

Variables	Univariate			Multivariable		
	Factor	95%Ci	p value	Factor	95%Ci	p value
After 6 MWT						
SpO2 (%)	13.04	-2.42 to 28.51	0.097	1.76	-7.28 to 10.79	0.7
PR (bpm)	0.09	-2.46 to 2.64	0.946	-0.52	-1.98 to 0.94	0.484
MAP (mmHg)	-2.37	-5.28 to 0.54	0.109	0.65	-1.11 to 2.41	0.466
Distance walked in six minute (m)	2.1	1.82 to 2.37	< 0.001	2.12	1.83 to 2.4	<0.001

CI: Confidence Interval, Statistical significance at P value<0.005

Table 5 Correlation with SF-IPAQ versus subscales of SF-36

Variables	SF-IPAQ	
	r	p
Physical functioning (%)	0.804	<0.001
Energy-fatigue score (%)	0.771	<0.001
Emotional wellbeing score (%)	0.648	<0.001
Social functioning (%)	0.49	<0.001
Pain score (%)	-0.799	<0.001
General health score (%)	0.658	<0.001
Health change score (%)	0.781	<0.001

r: Pearson correlation coefficient, Statistical significance at p value<0.005.

Our univariate regression analysis unveiled significant associations between all categories of SF-36 and the SF-IPAQ as follows: Each one unit rise in functionality, energy-fatigue, emotional wellbeing, social function, health status, and health change scores led to corresponding increases in the SF-IPAQ score, 1383.76 (95%CI: 1178.2 -1589.32), 817.63 (95%CI: 682.69 -952.56), 892.2 (95%CI: 681.56 -1102.85), 503.35 (95%CI: 324.54-682.15), 995.79 (95%CI: 767.02-1224.56) and 1036.25 (95%CI: 870.95 - 1201.55) by p<0.001. In contrast, for each one unit rise in pain, there was a corresponding decrease in the SF-IPAQ scores by -610.13 (95%Confidence Interval:-702.56 to-517.7) with p < 0.001.

According to regression tests, social function, pain and health scores emerged as the unique variables meaningfully related with the SF-IPAQ. Specifically, for every one unit rise in social function and health change score, the SF-IPAQ scores exhibited an increase of 157.62 (95%CI: 42.58- 272.67) and 266.45 (95%CI: 51.08-481.82) respectively, with p values of 0.008 and 0.016. As contrary, each one unit rise in pain scores led to a decrease in the SF-IPAQ scores with 269.43 (95%CI:-384.9 to -153.97), (p<0.001), (Table 6).

Discussion

In this research, we investigated the correlation between functionality, life quality, and physical activity levels among cases who underwent heart surgery, using the SF-IPAQ as a measure. Our findings revealed a significant, positive correlation with functional ability and physical performance, besides physical performance and life quality. Moreover, our results point that increased physical activity is related with improved functional

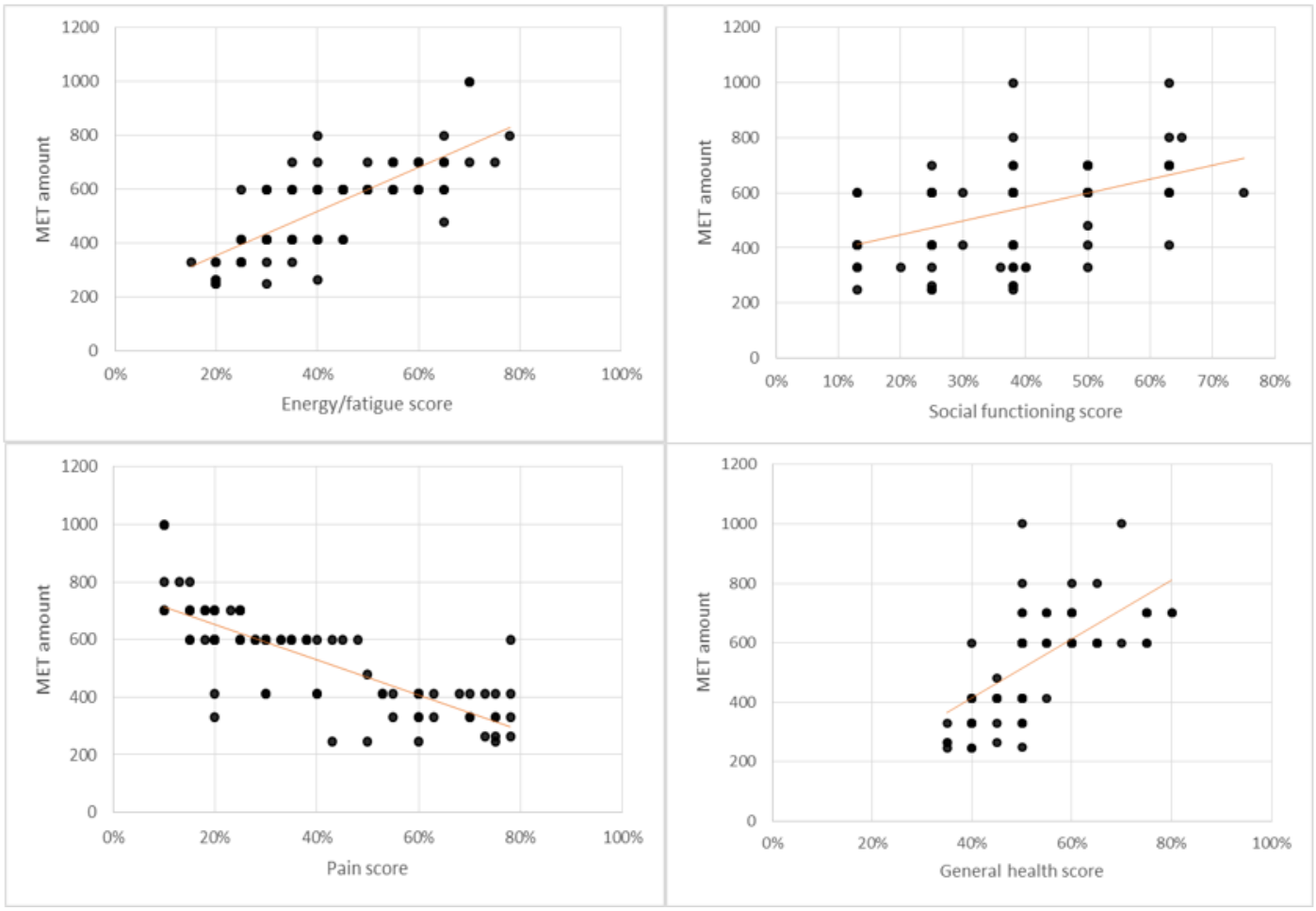

Figure 1 – Indicating the interrelation between energy/fatigue, social functioning, pain, general health and M.E.T measure

Table 6 Linear regression analysis of the relation of SF-IPAQ versus subscales of SF-36

Parameter	Univariate			Multivariable		
	Factor	95%Ci	p	Factor	95%Ci	p
Physical function (%)	1383.76	1178.2 to 1589.32	< 0.001	329.22	-15.65 to 674.08	0.061
Energy-fatigue (%)	817.63	682.69 to 952.56	< 0.001	168.84	-24.7 to 362.38	0.087
Emotional well-being (%)	892.2	681.56 to 1102.85	< 0.001	111.35	-81.59 to 304.29	0.255
Social functioning scores (%)	503.35	324.54 to 682.15	< 0.001	157.62	42.58 to 272.67	0.008
Pain scores (%)	-610.13	-702.56 to -517.7	< 0.001	-269.43	-384.9 to -153.97	< 0.001
General health status (%)	995.79	767.02 to 1224.56	< 0.001	-100.97	-329.12 to 127.18	0.382
Health change scores (%)	1036.25	870.95 –to 1201.55	< 0.001	266.45	51.08 to 481.82	0.016

CI: Confidence Intrval, Statistical significance at p value<0.05

ability and quality of life. Specifically, among the participants, comprising 37% with low physical activity levels and 63% with moderate levels, heightened physical activity was linked to enhanced functional capacity and life quality. Our research's conclusions suggest that while SF-IPAQ scores were inversely related to pain levels, they exhibited positive associations with energy-fatigue, social function, health, functionality and cognitive well being.

Functional capacity serves as a critical tool in clinical assessments, prognostic classification, and exercise prescription within the realm of cardiovascular diseases. Diminished exercise capacity stands out as a significant precursor in determining mortality. A recent study identified a robust and significant correlation between the resumption of physical activity within thirty days post-heart surgery and the subsequent quality of life [20]. This correlation was reported significantly interrelated with the life quality. While this study assessed the scores of the SF-36 and SF-IPAQ on the 7th day post-operation, they evaluated life quality using the life quality in cardio-vascular surgery test thirty days after surgical procedures. A randomized clinical trial conducted on post-surgery coronary artery patients reported a notable disparity in the average points of all life quality components before and after physical performance intervention in the experimental group [21]. Nevertheless, no difference was reported in the average scores of the 7 life quality components in the control group, both first and 4 months after discharge from surgical procedures. Our study's findings aligned with theirs concerning the test of physical activity and life quality on the 7th day post-surgery within a single group. However, their study evaluated physical activity level and life quality in two groups during the 1st and 4th months post-discharge from surgical procedures.

In a review study, it was reported that increased physical activity during spare time was related with higher scores across health-related quality of life dimensions [22]. These dimensions encompassed physical functioning, mental health, and vitality for both genders, while social functioning was specifically linked to women. Each dimension was assessed independently. Notably, the vitality component exhibited an increase of 0.17 and 0.39 points in men and women, respectively, with every additional hour per week spent in leisure-time physical activity. For the period that their research examined spare time, physical performance and life quality over a 3 years duration following heart surgery, our study identified a strong association with increased physical activity and improved life quality within the initial week post-cardiac surgery. This correlation, albeit modest, aligns with our findings indicating that heightened physical activity is linked to enhanced quality of life. However, a randomized controlled trial stated no meaningful differences in life quality between intervention groups at the day of hospital discharge [23]. These findings contrast with our findings regarding the SF-36 subscale scores, that indicated an increase in SF-36 subscales related with higher SF-IPAQ scores among cases that undergone cardiac surgery. This discrepancy can be attributed to the differences in the therapeutic interventions employed in the two studies. In another study, following cardiac surgery, cases underwent early mobilization facilitated by therapists. These sessions included instruction in breathing-coughing and walking exercises aimed at ensuring optimum oxygenation, secretion clearance, avoidance of respiratory tractus infections, and enhancement of endurance and functionality. However, the outcomes of this research revealed poor life quality results one month after hospital discharge [24]. In contrast, our study found that patients who underwent early rehabilitation achieved satisfactory results in terms of life quality.

Generally, the initiation of cardiac rehabilitation and prevention therapies is delayed to at least four to six weeks following hospital discharge [25]. However, literature indicates that individuals that undergone non-complicated myocardial infarction may derive benefits from early commencement of aerobic exercise performing, instantly one week post-discharge, to maximize anti-restructuring advantages. Moreover, it is advised that such patients persist with aerobic training tutoring for over to 6 month [26]. The 6MWT serves as a straightforward approach for evaluating cardio-pulmonary function. The outcome of metaregression analysis failed to demonstrate any notable correlation between alterations in 6MWT and either the onset time or duration. [27]. Hirschhorn et al. demonstrated that both the walking, walking-breathing exercise groups exhibited significantly longer 6MWT distances compared to the usual experimental group upon discharge from the hospital. Furthermore, during the inpatient period following coronary artery bypass grafting, a monitored moderate-intensity walking program overseen by a physiotherapist may augment functional capacity upon hospital departure [28]. This aligns closely with our own findings. In a quasi-experimental study, early implementation of physical activities including pulmoner exercises, incentive spirometer usage, coughing exercises and early mobilisation exercises resulted in meaningful improvements in hemo-dynamic factors and 6-MWT distance among post-heart surgery patients [29]. This finding corroborates our study's results, indicating a positive association between enhanced functional capacity and increased physical activity levels. Notably, our study observed this correlation within one group, assessing functional capacity and physical activity on the seventh day post-surgery, whereas their investigation examined these variables across two groups after the 12th week post-discharge. A potential limitation of our study lies in its focus solely on data from the initial 7 days post cardiac surgery. Expanding the follow-up duration in future research endeavors within this domain would bolster the robustness of our conclusions.

The principal limitations of this research stem from its single-center design and restriction to a single geographic location. Additionally, the exclusion of patients undergoing palliative revascularization may have constrained the breadth of our findings, precluding a comparison of quality of life outcomes between those receiving optimal revascularization and those undergoing palliative procedures. While acknowledging these constraints, it's crucial to state that the findings of our research may not be universally applicable to all cases undergoing CABG surgery in Iraq. Nonetheless, they serve as a foundation for informing the development of therapeutic strategies aimed at enhancing the quality of life for this patient population. Furthermore, within our study, we assessed functional capacity using the 6MWT, a submaximal evaluation method. Incorporating peak oxygen consumption, recognized as the gold standard for assessing exercise capacity, will enhance the objectivity of our presentation regarding changes in functional capacity.

Conclusion

Enhanced physical activity among post-operative cardiac patients is positively influenced by early mobilization and functional exercises. Following cardiac surgery, patients' functional capacity experiences positive effects from early mobilization and engagement in functional exercises. The significant benefits derived by patients who had cardiac surgery from early mobilization and functional exercises underscore the importance of actively encouraging their participation in these activities post-surgery. Early initiation of physical activity contributes to improved quality of life in post-surgical cardiac patients. Our findings suggest a direct correlation with increased physical activity and enhanced life quality alongside improved functionality. Also, this study observed the effectiveness of the early mobilization program on functional capacity, a crucial determinant of mortality among post-cardiac surgery patients.

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Predicting New-Onset Atrial Fibrillation in Patients with Coronary Artery Bypass Graft: the Precise-Dapt Score

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Abstract

Aim: Postoperative new-onset atrial fibrillation (POAF) after isolated coronary artery bypass graft surgery (CABG) is associated with adverse events. The Predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score is used to predict the bleeding risk after dual antiplatelet therapy and has been associated with arrhythmias in recent years. Therefore, the present study sought to investigate the association between the PRECISE-DAPT score and POAF after coronary artery bypass graft surgery.

Materials and methods: 350 patients who underwent CABG were retrospectively screened. After exclusion criteria, 135 patients were included in the study. A total of 135 patients who underwent on-pump CABG were divided into two groups: patients with POAF and those without POAF. The PRECISE-DAPT score was calculated for each patient, and intergroup comparisons of the calculated scores were performed.

Results: POAF was detected in 66 patients out of 135. Patients with POAF had longer hospital stays. PRECISE-DAPT score was higher in the patients with POAF compared to the patients without POAF ($p<0.001$). PRECISE-DAPT score was determined to be a predictor of POAF after CABG (odds ratio [OR]: 1.305; 95% confidence interval [CI]: 1.268–2.030; $p<0.001$). The PRECISE-DAPT score for POAF risk had a sensitivity of 60% and a specificity of 79% at cut-off values of 14.5 and above.

Conclusion: An increased PRECISE-DAPT score may be used as a predictive score for POAF that may develop during hospital stay after on-pump CABG.

Keywords: PRECISE-DAPT score, atrial fibrillation, coronary artery disease, hospital stay

Introduction

Coronary artery bypass grafting (CABG) is the preferred treatment over risk percutaneous coronary intervention in cases of advanced triple vessel disease or severe left main disease [1]. However, CABG may be associated with postoperative cardiac or noncardiac complications such as cognitive impairment, mortality, prolonged hospital stay, and arrhythmias [2].

Postoperative new-onset atrial fibrillation (POAF) is commonly observed arrhythmia after isolated CABG [3]. POAF is associated with prolonged hospital duration, stroke, repeated hospitalizations, and early or late mortality. In addition, similar to nonvalvular atrial fibrillation (AF), POAF poses a thromboembolic risk [4]. The complications that may be noted in patients with AF do not vary between short-term or permanent forms of AF [5].

The predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score is designed to predict bleeding complications in patients undergoing stent implantation who are subsequently treated with dual antiplatelet therapy [6]. Previous studies have shown that the PRECISE-DAPT score is related to mortality, arrhythmic complications, and thrombus [7-9].

Based on the above information, POAF may have clinical significance after CABG. The PRECISE-

DAPT score, which includes parameters known to be linked with AF, such as age and kidney failure, is likely associated with POAF after CABG. As far as we know, the relationship between the PRECISE-DAPT score and POAF in patients undergoing CABG has not been investigated yet. Therefore, this study aimed to investigate this relationship.

Material and methods

Study population

We retrospectively screened every consecutive isolated CABG surgery patients at a tertiary healthcare center, between January 2013 to February 2022. Local ethics committees approved the study (dated: March 02, 2022, project number: 2011-KAEK-27/2022-2200038254). Helsinki Declaration was followed at all stages of the study. The retrospective design of this study did not permit the participants to provide written informed consent up front.

We screened 350 patients (CABG or combined valve replacement and CABG) within the study period. Patients' CABG procedures were performed in our center, and patients who came for regular check-ups for at least 6 months after discharge were included in the study. 215 patients were excluded due to not meeting the inclusion criteria. Group 1 consists of 66 patients with POAF and Group 2 is composed of 69 patients without POAF. POAF was defined as atrial arrhythmia that did not exist before CABG and that lasted at least 30 min with the absence of visible P waves and presence of irregular RR intervals on 12-lead electrocardiography after CABG. Each patient with POAF was anticoagulated and received cardioversion (electrical or medical) to restore the sinus rhythm.

The PRECISE-DAPT score for patient was determined using the following online tool: http://www.precisedaptscore.com. The score was calculated using five clinical parameters (i.e., age, white blood cell count [WBC], hemoglobin level, history of spontaneous bleeding and creatinine clearance) [10].

The exclusion criteria were having a history of CABG or valve surgery, left ventricular ejection fraction ≤40%, history of stroke, renal failure (eGFR < 30 ml g/1.73m2), active infection, a diagnosis of malignity, chronic pulmonary embolism, a diagnosis of pulmonary hypertension, regular alcohol consumption (>20 g/day), a diagnosis of chronic obstructive pulmonary disease, permanent pacemakers, moderate to severe heart valve disease, history of AF, flutter history or history of successful ablation, thyroid dysfunction; undergoing surgery because of failed percutaneous coronary intervention; and being younger than 18 years.

Left ventricular ejection fraction (LVEF) ≤ 40% were classified as having heart failure with reduced left ventricular function [11]. Patients who were diagnosed with COPD as defined in the literature [12], were in the stable phase of the disease, and received the same treatment for the last 3 months were defined as COPD patients. Active bleeding is defined as bleeding beyond 1.5 ml/kg/hour for six consecutive hours in the first 24 hours [13].

An experienced cardiologist performed the coronary angiography (GE Healthcare Innova 2100, New Jersey, USA). The angiographic images were reviewed by an experienced cardiologist and cardiovascular surgeon. To identify surgical indications, the current guidelines were followed [14].

All patients were taken to operating room and monitored a complete hemodynamic monitoring system including five-lead electrocardiography, central venous catherization and peripheral oxygen saturation. Midazolam, sevoflurane and fentanyl were used for anestesia protocol. All patients underwent on-pump CABGs through a median full sternotomy. Patients were heparinized with 300-400 IU/kg intravenously to achieve an activated clotting time 400-450 s before cannulation. We performed traditional ascending aortic cannulation and 2-stage right atrium venous cannulation. After clamping nonpulsatile roller pump maquet hl 30 aorta antegrade warm cardioplegia were used. all anastomosis were performed after cardiopulmonary bypass. On-pump surgery was performed with the use of nonpulsatile HL 30 roller pump (Maquet, Rastatt, Germany) and membrane oxygenator (Medtronic TRILLIUM AFFINITY NT, Hollow Fiber Oxygenator, USA). Surgery was performed in hypothermia at 28 to 32 C with the use of anterograde warm blood cardioplegia. Maintenance cardioplegia was repeated every 20 minutes as antegrade cardioplegia (5 ml/kg). Proximal anastomosis was performed under side-clamp in all patients. After distal anastomoses cardiopulmonary bypass terminated. After decanulation heparin was neutralized with 1 mg protamine sulfate. In all patients, two drainage tubes were placed with a 28 F drain in the anterior mediastinum and a 30 F drain in the left thoracic cavity. In order to ensure the patency of the drains after surgery intensive care unit (ICU), a continuous suction pressure of 20 mmHg was applied and the drains were removed intermittently. Continuous follow-up was provided during the two-day period that the patients were followed in the ICU, and rhythm problems were recorded using a standard 12-lead electrocardiogram in patients who developed rhythm problems.

Statistical analysis

We conducted power analysis using G-Power 3.1.9.7, determining a minimum requirement of 128 subjects based on an effect size of 0.50, a margin of error of 0.05, and a desired power of 0.80 (80%) (t tests were analyzed for the difference between two independent means (two groups) from the main component). Data were analyzed with SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Kolmogorov–Smirnov test was performed to assess the distribution of continuous variables. The continuous variables obtained in the analysis were expressed as means ± standard deviations; the categorical variables were expressed as percentages and numbers. To compare normally distributed and nonnormally distributed parameters, Student's t-test and Mann-Whitney U test were utilized, respectively. Chi-square tests compared probability ratios of categorical variables. For correlation analysis, Pearson's test was used. A univariate logistic regression analyzed independent predictors of POAFThe variables that showed statistical significance were further analyzed using multivariate logistic regression. A Youden Index was used to find the cutoff value of PRECISE-DAPT score. Receiver operating characteristic (ROC) curve analysis was employed to predict POAF using the PRECISE-DAPT score and its individual components. Significant P-values were considered to be less than 0.05.

Results

135 patients were included in our study. Antiarrhythmic drug treatment to prevent arrhythmia was not started in all patient groups before the procedure. Statistical differences were detected between groups in triglyceride levels (p=0.048) and red cell dist ribution width (RDW) (p=0.020) (Table 1).

Table 1 Comparison of baseline clinical and demographic characteristics of groups

Variables	POAF (+) (n=66)	POAF (-) (n=69)	P value
PRECISE-DAPT score	16 (12-24.75)	12.5 (6-19)	<0.001
Age (years)	64.14±9.45	61.01±9.92	0.064
Gender (n) (%)			0.540
Male	50 (75.8)	48 (69.6)	0.920
Female	16 (24.2)	21 (30.4)	0.511
BMI (kg/m^2)	25.09±1.45	24.93±1.62	0.537
Smoking (n) (%)	31 (47)	30 (43.5)	0.684
Hypertension (n) (%)	41 (62.1)	40 (58)	0.623
Diabetes mellitus (n) (%)	21 (31.8)	18 (26.1)	0.586
History of CAD (n) (%)	13 (19.7)	9 (13)	0.416
COPD (n) (%)	10 (15.2)	8 (11.6)	0.723
Dyslipidemia (n) (%)	10 (15.2)	7 (10.1)	0.537
Prior bleeding (n) (%)	3 (4.5)	1 (1.4)	0.358
SBP (mmHg)	106.66 ±18.26	110.56±14.58	0.174
DBP (mmHg)	80.62±7.68	80.79±7.96	0.896
Heart rate (beats/min)	85.80±13.59	87.05±15.92	0.623
Laboratory Data			
Glucose (mg/dl)	113 (94.5-166)	119 (92-170)	0.417
Creatinine (mg/dl)	0.84±0.15	0.83±0.16	0.870
Glomerular filtration rate (mL/m)	90.26±25.19	90.66±25.54	0.928
Sodium (mmol/L)	139.45±3.65	138.49±3.13	0.103
Potassium (mmol/L)	4.13±0.40	4.03±0.47	0.208
AST (U/L)	24.48±7.74	22.43±12.16	0.247
ALT (U/L)	22.71±8.56	20.49±7.30	0.107
Triglyceride (mg/dl)	114 (90.8-169.2)	140.25 (108.5-179.6)	0.048
HDL cholesterol (mg/dl)	44.0 (36.45-52.32)	43.20 (35.25-50.20)	0.614
LDL cholesterol (mg/dl)	114.70 (77.97-160)	119.10 (91.5-151.7)	0.617
Hemoglobin (g/dl)	12.89±2.15	13.34±1.31	0.132
WBC (µ x 103/µL)	8.21±2.09	8.24±2.18	0.930
Platelets (µ x 103/µL)	246.8±77.3	264.9±60.4	0.125
RDW (%)	14.72±1.29	13.90±2.62	0.020
Postoperative cardiac hsTnI, ng/L	62.25 (13.60-425.20)	48.5 (25.0-132.65)	0.237

CAD, coronary artery disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; COPD, chronic obstructive pulmonary disease; hsTnI, hihg-sensitivity troponin I; AST, aspartate aminotransferase; ALT, alanine aminotransferase; WBC, white blood cell; RDW, red cell distribution width; PRECISE-DAPT, predicting bleeding complications in patients undergoing stent implantation and subsequent dual anti platelet therapy; LAD, left anterior descending coronary artery; LCX, left circumflex artery; LDL-C, low-density lipoprotein cholesterol; RCA, right coronary artery; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; POAF, postoperative new-onset atrial fibrillation

Most patients had three-vessel disease. There were no patients with urgent diagnosis of CABG in the cohort. The mean duration of arrhythmia in Group 1 was 21.94 ± 5.73 hours. There was one patient with active bleeding and the patient was re-operated (Table 2). There was correlation between the duration of POAF duration times and the PRECISE-DAPT score ($r = 0.596$; $p < 0.001$).

Table 2 Echocardiography and procedural characteristics of groups

Variables	POAF (+) (n=66)	POAF (-) (n=69)	P value
Echocardiography Data			
LVEF (%)	48.66±5.57	50.55±6.52	0.039
LVEDD (mm)	40.74±9.05	39.21±8.70	0.567
LVESD (mm)	38.06±6.35	38.05±5.47	0.954
LA diameter (mm)	44.84±8.00	45.02±8.61	0.925
Previous medications			
Asprin	33 (50.0)	28 (40.6)	0.272
Statin	14 (21.2)	11 (15.9)	0.571
Beta-blocker	13 (19.7)	18 (26.1)	0.498
ACE inhibitors/ARB	41 (62.1)	40 (58)	0.623
Culprit lesions			
3-vessel disease	52 (78.8)	47 (68.1)	0.227
Left main disease	6 (9.1)	4 (5.8)	0.464
Intra-op and post-op data			
Total pump time	123.0±18.04	116.44±13.57	0.018
Aortic cross-clamp time	91.66±17.07	84.04±14.77	0.007
Duration of ICU	5.11±2.55	3.88±1.76	0.001
Ventilation time	25.0±1.84	23.60±1.98	<0.001
Duration of hospital stay	16.84±6.45	14.36±5.51	0.021
Postoperative iv inotrope	5 (7.6)	2 (2.9)	0.267
Duration of POAF (hours)	21.94±5.73	-	-
In-hospital bleeding	5 (7.6)	2 (2.9)	0.267
Bleeding requiring revision	1 (1.5)	(0)	0.489

LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LA, left atrium; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ICU, intensive care unit; POAF, postoperative new-onset atrial fibrillation

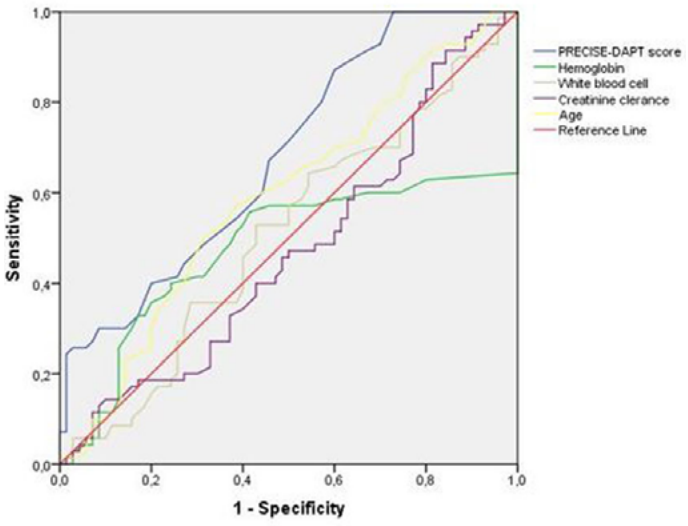
Univariate regression analysis identified RDW, postoperative cardiac hihg-sensitivity troponin I (hsTnI) level, aortic cross-clamp time, total pump time, and PRECISE-DAPT score significant predictors of POAF. In the multivariate analysis, postoperative cardiac hsTnI level and PRECISE-DAPT score were significant predictors of POAF (Table 3).

Table 3 Logistic regression analysis of new-onset AF-related clinical parameters

Variables	Univariable OR (95% CI)	p-value	Multivariable OR (95% CI)	P value
Age	0.967 (0.933-1.002)	0.066		
Diabetes mellitus	0.756 (0.359-1.595)	0.463		
Hypertension	0.841 (0.422-1.677)	0.623		
Dyslipidemia	0.632 (0.225-1.773)	0.384		
Smoking status	0.868 (0.441-1.712)	0.684		
LVEF	1.053 (0.995-1.115)	0.076		
LA diameter	1.002 (0.962-1.044)	0.924		
RDW	0.768 (0.590-0.999)	0.049	0.855 (0.652-1.121)	0.257
Triglyceride	1.001 (0.997-1.006)	0.522		
Postoperative cardiac hsTnI	0.997 (0.995-0.999)	0.006	0.984 (0.991-0.997)	0.018
Aortic cross-clamp time	0.969 (0.947-0.992)	0.009	0.975 (0.935-1.016)	0.226
Total pump time	0.974 (0.952-0.996)	0.022	0.995 (0.954-1.038)	0.812
PRECISE-DAPT score	0.995 (0.954-1.038)	<0.001	1.305 (1.268-2.030)	<0.001

Abbreviations are given in tables 1 and 2.
OR, odds ratio; CI, confidence interval

The area under the curve values of the PRECISE-DAPT score and its components (hemoglobin, WBC, creatinine clearance, and age) were 0.68 (95% confidence interval or CI 0.59–0.76) for POAF (+) (Figure 1). In patients undergoing CABG, the PRECISE-DAPT score was better at predicting POAF than all components combined (hemoglobin 0.47, 95% CI 0.37–0.57; WBC count 0.51, 95% CI 0.41–0.60; creatinine clearance 0.47 (0.37–0.56).and age 0.58, 95% CI 0.49-0.68). HsTnI level was 0.55 (95% confidence interval or CI 0.45–0.65) for POAF (+) (p = 0.237).



	AUC	95% CI	P-value
PRECISE-DAPT score	0.68	0.59-0.76	Reference
Hemoglobin	0.47	0.37-0.57	0.629
White blood cell	0.51	0.41-0.60	0.845
Creatinine clearance	0.47	0.37-0.56	0.567
Age	0.58	0.49-0.68	0.068

Figure 1 – Receiver operating curves (ROC) to predict POAF in patients with CABG

The PRECISE-DAPT score for POAF risk had a sensitivity of 60% and a specificity of 79% at cut-off values of 14.5 and above.

Discussion

Our study's has significant findings: (1) Group 1 had significantly higher PRECISE-DAPT scores than Group 2; (2) POAF duration time strongly correlated with the PRECISE-DAPT score; (3) the postoperative cardiac Tn level and PRECISE-DAPT score were found to be the predictors of the development of POAF after CABG.

The PRECISE-DAPT score independently predicts arrhythmias such as ventricular tachycardia, atrial fibrillation (AF), and new-onset AF [8,15]. POAF is a common arrhythmia after CABG and is associated with complications such as disability and mortality. Although it is affected by various factors such as age, obesity, diabetes mellitus, and hypertension, its pathophysiology remains unclear [2]. POAF developing after CABG may be associated with left atrium dilatation; its incidence is often higher in men. Increased sympathetic activation is an important trigger for POAF [16] and beta blockers were used in equal percentage in both groups before the surgery, our results vary from those available in the literature.

A correlation has already been identified between POAF after CABG and aortic cross-clamp time. POAF develops due to ischemia-reperfusion injury triggered by increased cross-clamp time and ectopic activity induced by the increased inflammatory infiltrates in the atrial tissue [17]. In our study, group 1 exhibited significantly longer aortic cross-clamp times. Although univariate analysis identified aortic clamp duration as a predictor of POAF, similar results were not obtained in multivariate regression analysis. Our results differ from those reported in the literature; this deviation may be because our study population comprised patients who underwent isolated CABG, not CABG or valve surgery.

In a study investigating inflammatory processes, increased RDW values in patients with acute coronary syndrome have been reported to predict new-onset AF [18]. In our study, Group 1 had significantly higher RDW than Group 2. Based on the demographic data of the cohort, the younger age range of the patients in this study might have led to results inconsistent with those reported in the literature (of nearly 70 years). In light of the abovementioned information, it can be said that the etiology of POAF remains unclear and the clinical parameters remain uncertain.

In our study, the PRECISE-DAPT score identified patients with a risk of developing POAF after CABG. Moreover, patients with high PRECISE-DAPT scores require closer follow-up as the higher scores in these patients are associated with poor clinical outcomes such as increased ventilation time, longer stay in the intensive care, and longer hospital stay.

Our study has some limitations, which primarily include the single-center design of the study and the small cohort size. In addition, all our patients underwent on-pump CABG and there were no off-pump CABG cases.

Conclusion

Patients who developed postoperative atrial fibrillation (POAF) after on-pump CABG tended to have higher PRECISE-DAPT scores. This suggests that an increased score could independently predict the development of POAF in these patients undergoing on-pump CABG.

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The Prevalence of Different Genotypic Forms of Familial Hypercholesterolemia in Relation to Race and Ethnicity

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Abstract

In the present study, a systematic literature review was conducted to evaluate the epidemiology of Familial hypercholesterolemia genetic variants according to different ethnic and racial background. Familial hypercholesterolemia (FH) is an inherited disease characterized by severe dyslipidemia and as a result high cardiovascular risk. Lipid profile of this patients distinguishes with increased cholesterol and low-density lipoprotein (LDL) blood levels. Databases PubMed, Web of Science, and Elsevier were searched and only peer-reviewed articles with a large number of contributors and sufficient prevalence and ethnicity data were included. Diagnosis of FH was based on genetic testing or clinical criteria. The results of the study indicate inadequate and untimely diagnosis of FH, resulting in inadequate treatment. To date, only 9% of countries have statistical data on the FH prevalence among their citizens. In order to develop effective prevention strategies for cardiovascular diseases associated with FH, further research is needed to obtain accurate epidemiological data, including the race and ethnicity of patients. This will allow to optimize strategies for reducing the social-economic burden of preventable cardiovascular disease associated with FH.

Keywords: Familial hypercholesterolemia, cardiovascular disease, low-density lipoprotein, genes.

Introduction

Familial hypercholesterolemia (FH) is an inherited autosomal dominant disease associated with elevated levels of total cholesterol and low-density lipoprotein (LDL) in the blood. As a result of dyslipidemia, patients have increased risk of atherosclerotic cardiovascular disease early development. Familial hypercholesterolemia characterized by quite complex genetics. It can be subdivided for two main forms: homozygous (mutation in both alleles, severe clinical prognosis and outcome) and heterozygous (presence of mutation in one allele, more favorable outcome). In this case, depending on the combination of mutations, the presence of monogenic or polygenic nature of the lesion distinguishes true homozygous form, as well as combined and compound heterozygotes. Substantially, all cases of FH are induced by mutations in genes, which encode LDL receptors, proprotein convertase subtelisin/kexin 9, Apo B protein. The reason for the rare autosomal recessive form of familial hypercholesterolemia is LDLR1 gene mutation. LDL receptor gene mutations are responsible for 85-90% of genetically confirmed cases of FH [2]. Currently, more than 4900 variants of the LDLR gene and about 350 variants of the PCSK9 gene have been identified, but the pathogenetic significance of most of them has not been proven [29].

According to the data from epidemiology studies, the prevalence of two genetic forms (homozygous and heterozygous) differs significantly. Homozygous familial hypercholesterolemia (homoFH) is a very rare disease, for a long time the incidence was estimated at 1: 1,200,000 populations, but according to a more in-depth study in some European countries (Netherlands, Italy, Spain) it was re-estimated as 1: 650,000, and then 1: 160 - 300,000 [8].

Heterozygous familial hypercholesterolemia (heFH) is one of the most common genetically determined pathologies in the world. According to recent studies, its prevalence is 1:250 in the United

States [1], 1:192 in Catalan Spain, and at 1: 137 in the Danish population [22].

Most studies suggest that familial hypercholesterolemia remains an inadequately and untimely diagnosed pathology, which consequently leads to untimely and incomplete treatment. With an expected number of about 34 million patients worldwide, less than 1% are currently identified in most countries [9,10]. Only 9% of countries in the world have accurate statistics of FH epidemiology [1]. But until this moment prevalence of FH in dependence to the different ethnic groups is not clearly estimated. Obtaining more accurate epidemiological data, including race and ethnicity of patients, will help to optimize strategies to decrease the burden of preventable cardiovascular diseases (CVD).

Purpose: To develop an understanding of the homo- and heterozygous hypercholesterolemia prevalence according to different racial and ethnic groups, and to identify gaps in its epidemiology and demographic characteristic in order to identify future research directions

Materials and methods

A search for relevant to the study topic publications was performed via PubMed, Web of Science, and Elsevier databases from inception to December 2022 reporting on the prevalence of familial hypercholesterolemia among different ethnic groups.

All peer-reviewed published articles [1] involving more than 100 participants in a study with relevant prevalence and ethnicity were considered suitable for inclusion as illustrated in Figure 1 [2]. For diagnosis of FH one of the following criteria was used: genetic testing, Dutch Lipid Clinic Network clinical criteria, Simon Broome criteria, MEDPED (Make Early Diagnosis to Prevent Early Death).

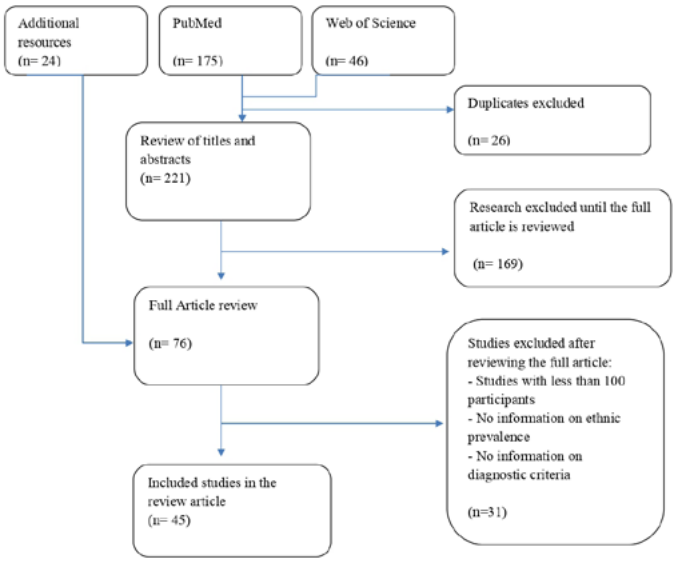

Figure 1 – Study selection flowchart

Studies with unclear methodology for obtaining FH prevalence were excluded.

In the analyzed publications, the epidemiology and prevalence of homozygous familial hypercholesterolemia were evaluated both on the basis of the general population studies and on the basis of Hardy-Weinberg principles calculations. The assessment and analysis of the studies are presented in the Table 1.

Table 1 Assessment and analysis of the studies

Title	Country	Publication year	Data source	Age	Period of participants' inclusion	Diagnostic criteria for FH
ELSA-Brasil study	Brazil	2018	Population study	35-75	Not indicated	DLCN
NHANES study	USA	2016	Population study	>18	1999-2012	DLCN
	USA	2018	Population study	>20	1999-2022	Modified DLCN II
Cape Town Experience	South Africa	2008	Population study	>50	2011-2019	DLCN
YOUNG-MI Registry	USA	2019	Retrospective study	41-50	Not indicated	Not indicated

FH – Familial hypercholesterolemia.
DLCN – Dutch Lipid Clinic Network.

Table 2 Racial and ethnic groups

Region	Ethnic groups
Europe	Danish, Dutch, French, Hispanic, Italian, German, Polish
East Asia	Arabian, Druze, Kurds, Persian, Turks, Jews
Southwest Asia	Chinese, Japanese
Africa	African
North America	Canadian
South America	Brazilian

The following keywords were used in the search: homozygous and heterozygous familial hypercholesterolemia or LDLR or apolipoprotein B or gene mutation, ethnic group or racial and ethnic prevalence. All the racial and ethnic groups are listed in the Table 2.

Results

Over the last decades, a number of studies have demonstrated significant differences in the FH epidemiology not only between countries but also among different ethnic and racial groups. This difference can be determined by several factors: using of different diagnostic criteria [32], differential access to medical care and to genetic testing, differences in screening approaches [11], and differences in the methodology of inclusion of representatives of different ethnic populations, and also due to the "founder effect" in some countries.

To date, almost all studies of the FH prevalence have come from countries on the European continent, North America, East Asia and Australia. This problem is practically unstudied in the African continent, South America, and the Asian region. Moreover, the authors most often studied the prevalence of heterozygous forms, while the demography of homozygous hypercholesterolemia is described in a few papers.

European scientists have pioneered the epidemiology of familial forms. The first large-scale study of the FH prevalence was published in 2012, based on a non-selective Danish population of >69 000 individuals. The prevalence of verified/probable FH was 1:137 [22]. In 2016, the same authors

conducted another study including >98,000 individuals, the prevalence of familial forms of conditional mutations in LDLR and Apo B genes was 1:217 [35]. In other European countries, the prevalence of SHCC was roughly comparable: Poland 1:247 (meta-analysis of 6 studies, 38,900 participants), the Netherlands 1:319, and Germany 1:295 [36, 37, 38]. At the same time, FH was significantly less frequent in the Italian population - 1:526 (for diagnosis the criteria of the Danish lipid clinics were used) [39].

Most of the earlier studies included only Caucasian and Negroid individuals. Several studies, which were later included in meta-analytical projects, investigated the prevalence of FH, including Asian and Hispanic populations. It is noteworthy that there are quite pronounced variations in prevalence values according to different studies, even in ethnically similar populations.

One of the earliest meta-analyses with a broad geography of included studies is the analysis published by Akioymen et al. in 2017. The meta-analysis included 19 cohorts: 9 in Europe, 4 studies from North America, 2 Asian cohorts, 3 studies conducted in the Australian continent and 1 in the African continent [34]. The expected prevalence in each cohort vary from 0.05% to 5.62%. The overall prevalence across the combined population was 0.40% (1:250 individuals, with 95% confidence interval). This analysis has series of limitations: the differences in selected population, design and methods of research, diagnostic criteria for FH. These factors resulted in marked heterogeneity of the included studies.

National Health and Nutrition Examination Surveys (NHANES) study

More recently, in 2020, the results of a large-scale meta-analysis and systematic review on the prevalence of familial forms of hypercholesterolemia in different ethnic groups were published. Meta-analysis consists of thirteen studies, the total number of participants was 1,169,879, and the overall prevalence of FH was 1:303, which is consistent with other authors [7]. The studies included in the meta-analysis predominantly reflected the prevalence of familial forms in a single ethnic group, and only a few studies examined multiple cohorts. Specifically, the National Health and Nutrition Examination Surveys (NHANES) study included members of the following racial groups: non-Hispanic Negroid race, non-Hispanic Caucasoid race, non-Hispanic Mexican-American, and Hispanic. The overall prevalence of familial hypercholesterolemia was 0.40% or 1:250 [1].

ELSA-Brazil study

The ELSA-Brazil study, which included 15,101 Brazilian citizens aged 35-74 years, was based on racial groups such as Negroid, Caucasian and Hispanic. Asian race was excluded due to the small population of this ethnic group in Brazilian territory [23]. The FH overall prevalence was 0.38% or 1:263 [2]. Detailed analyses showed that prevalence of FH increased from 1:417 in the Caucasian cohort, 1:204 among Hispanics to 1:156 in the Negroid cohort. Such high prevalence figures for FH among the Negroid and Hispanic races indicate how underestimated this problem is, both locally and globally.

Pooled data on ethnic prevalence of FH from different studies show higher values among the Negroid race compared to the overall population. In the NHANES study it was 0.46% or 1:249, and 0.64% (1:156) in the ELSA-Brazil study, respectively. At the same time, according to the data of NHANES study, prevalence of FH among individuals with mixed ethnicity and/or race (0.28% or 1:357) was lower than in the general population. The prevalence of FH was also lower in the Caucasian population at 0.25% (1:417) [2].

Cape Town Experience study and YOUNG-MI Registry study

Two studies (Cape Town Experience and YOUNG-MI Registry) have focused on the prevalence of FH by race among so-called "patient" groups. These are cohorts in which participants were recruited among patients in lipid clinics or hospitals, or had high lipid values and/or prior cardiovascular disease. Expectedly, the prevalence of familial forms was higher in these cohorts than in the overall population, while ethnic differences persisted. The overall prevalence of familial heterozygous hypercholesterolemia was 23% [1:4] according to the Cape Town Experience (Cape Town, South Africa, 2008) [4] and 9% or 1:11 according to the YOUNG-MI Registry (USA, 2019) [5]. At the same time, comparison of the two studies results revealed marked differences in the FH prevalence in ethnic groups. In particular, in the Cape Town Experience study, the highest prevalence was observed among Caucasians (32% or 1:3) and Asians (20% or 1:5). YOUNG-MI Registry data showed a high prevalence of this nosology in the Hispanic patient cohort, 14% or 1:5, while in the Asian cohort the values were significantly lower than in the general population, 4.3% or 1:23.

In 2020, the results of another large meta-analysis were published, which included 104 publications and about 11,000,000 patients, respectively, to estimate the prevalence of FH in several subpopulations. Specifically, 44 articles focused on the epidemiology of familial forms in the general population, 28 publications focused on patients with coronary artery disease, 32 studies assessed the prevalence of the FH in patients with early developed coronary heart disease and coronary events, and another 19 articles included patients with severe hyperlipidemia [15]. According to the results of a meta-analysis, in the general population the prevalence of familial hypercholesterolemia was 1:313, while in patient cohorts it was significantly higher: 10 times higher in patients with coronary disease and 20 times in patients with premature cardiovascular events. In the group of patients with severe hypercholesterolemia, the prevalence of familial forms was 23 times higher compared with the whole population [15]. The same meta-analysis compared the prevalence of hypercholesterolemia by ethnicity: Caucasian, Negroid, East Asian and Arab subpopulations.

In contrast to previously reported data in the above meta-analysis, the prevalence of FH in the Asian population was significantly lower than in Europe and North America, 0.19% and 0.32%, respectively. One explanation could be the genetic differentiation of different ethnicities. In addition, the studies by Japanese authors, also included in the meta-analysis, used the criteria for diagnosing CVD developed by the Japanese Atherosclerosis Society in 2012 [16], while most other authors from the Asian region used criteria developed for the Western world, which may affect the validity of the data, since members of the Asian ethnic group traditionally have lower lipid profiles [17].

However, in the patients sub cohorts with coronary pathology and early coronary events, the prevalence of FH among Asian ethnic groups was comparable with that in Europeans and "white" Americans - 3.6% and 5.75%,

respectively [15]. Over the past decades, a significant change in the characteristics of the lipid spectrum in Asian countries, including Japan and China, has been noted, in particular, an increase in the level of total cholesterol, which may be explained by changes in lifestyle [40]. A 2014 study in China using the adapted Danish Lipid Clinics criteria reported a prevalence of FH of 0.28% [42].

In recent decades, there has been a significant change in the demography of inherited diseases and in particular heterozygous and, to a greater extent, homoFH, due to the impact of migration flows on population growth in different regions and the emergence of new sources of mutations.

There are several countries and ethnic groups in the world that are predicted to have a significantly higher incidence of FH. In particular, as a result of the "founder effect" presence, such groups may include French-Canadians, Africans, Christian Lebanese, and ethnic Arabs [1,12]. "Founder effect" in genetics refers to a decrease in gene variability when a new population in a new area is formed by separating a very small group of individuals from a larger population [34].

Other studies

A higher prevalence of FH would also be expected in the Gulf countries (Bahrain, Kuwait, Iraq, Oman, Qatar, Saudi Arabia and the United Arab Emirates), given the greater frequency of closely related individuals. In 1995, a survey of 3212 families in Saudi Arabia was conducted, the percentage of close marriages was 57.7%, with cousins accounting for 28.4% of the couples (26). Almost 10 years later, this study was replicated. 600 women were interviewed, the presence of marriage with cousins was indicated by 30% of respondents, and in parental families this fact was noted by 23% of respondents, i.e. this tradition is preserved to this day [27]. In addition, the previously described "founder effect" is very pronounced in the Gulf countries, reinforced by the high frequency of inbreeding. In particular, Saudi Arabia is home to the mutation of exon 14 of the LDLR gene, which occurs in 40% of the population [28]. Accurate data on the prevalence of FH in Saudi Arabia is not available at the moment, however, according to the Ministry of Health data for 2013, the dyslipidemia prevalence in the population was 8.5% [44]. Regarding FH, there is data from a study conducted in 2018, which included 3224 patients hospitalized for acute coronary syndrome, the prevalence was 3.7% [45]. At the same time, in Israel, another country in the Middle East region, according to the data from 685,314 insured citizens the prevalence of FH was comparable to the European population and compose 1:355. MEDPED criteria were used for diagnosis [41].

Another region in which the FH prevalence is significantly higher than the global rates is South Africa, in particular in 3 ethnic groups - Afrikaners (South Africans of European descent), Jews and South Asian Indians - it is 1:80 [30]. A study by Frederick J. Raal et al on the results of cascade screening in a South African population was published in 2020. The study included 700 subjects, 295 cases (42%) were index cases [32]. The study identified a very interesting ethnic group, 16 dark-skinned Africans, who were not found to have atherosclerosis-associated cardiovascular disease despite long-term exposure to high or extra high levels of LDL and often Lp(a), with a similar incidence of arterial hypertension and diabetes mellitus in non-dark-skinned Africans. This finding is an unexpected phenomenon that requires more detailed study. Ahmad et al. showed an inexplicably higher prevalence of autosomal dominant forms of FH among the non-Hispanic Negroid population. The low prevalence of LDLR gene mutations in the same ethnic group suggests an alternative mechanism of expression of the familial hypercholesterolemia phenotype in the African population [20].

The study of the ethnic peculiarities of the prevalence of FH and variations in its genetic substrate is of rather significant clinical importance, allowing to optimize treatment and diagnostic processes in local populations. In particular, the analysis of the Canadian register of FH, including data of patients from 2008 - 48 people, showed that compared to the world data in the Canadian cohort of patients among the clinical manifestations of the disease was dominated by aortic valve stenosis 47.9% of cases [21].

As in the case of heFH, the prevalence of homozygous forms was also re-evaluated as the results of cohort studies accumulated. In particular, in Denmark it was 1:160 000 [46], in the Netherlands genetically identified forms occurred with a frequency of 1:300 000 [37]. In the Spanish population, the incidence of homozygous FH was 1: 450,000 [47], while in Germany it was significantly lower than the European average of 1: 860,000 [48]. There have been few studies of ethnic aspects of the prevalence of homozygous forms; there are results of studies of a Japanese cohort, where homozygous forms were quite rare with a frequency of 1: 171,167 [49].

Given the need for early diagnosis of familial forms of hypercholesterolemia for the goal of as early as possible initiation of therapy and prevention of the development of significant cardiovascular events, much attention has recently been paid to the study of the epidemiology of FH among children and adolescents. Globally, it is estimated that 20-25% of all cases of FH occur in pediatric population, with 1 child born with this pathology every minute [50,51]. Belay et al. in a study on prescribing statin therapy to pediatric patients, including 885 participants, noted that 92% of the children were of Caucasian race. The general overview of racial differences is illustrated in the Figure 2 in Appendix. These figures reflect differential access to diagnostics and, including cascade screening, in the non-white population [19].

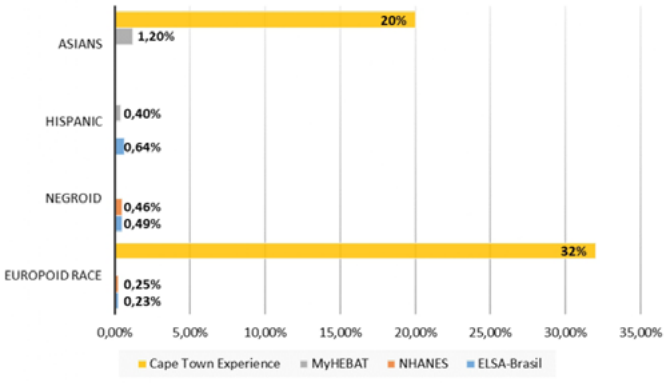

Figure 2 – Familial hypercholesterolemia prevalence by race and ethnicity according to studies

Discussion

Thus, analyzing all of the above, it can be concluded that despite a large number of studies, national screenings, and the development of new approaches, familial hypercholesterolemia remains an underdiagnosed disease. The prevalence of this

pathology in the general population remains unknown in approximately 90% of countries. The European continent is the most studied. According to the data presented, there is considerable variability in the epidemiology of familial forms between different ethnicities and continents. In particular, members of the Negroid race, according to most studies, have a high prevalence of FH. Members of the Asian race have traditionally been less likely to have FH, although there is a trend towards variation in this population as well. There are a number of populations with a very high prevalence of hypercholesterolemia, such as the Gulf States, French Canadians, Afrikaners, etc.

Adequate assessment of the prevalence of FH is difficult, also due to the lack of complete information. Currently available clinical and molecular diagnostic methods have their advantages and disadvantages. In the scoring scales of clinical criteria of FH, lipid arch of the cornea and xanthomatosis of the Achilles tendon have the maximum specific weight. However, according to a genetic cascade screening program conducted in Brazil, among patients with a confirmed gene mutation, these features were detected in only 28.4% and 13.2%, respectively [24]. On the other hand, genetic testing was able to identify the causative mutation in only 20-30% of patients with probable FH, and in 60-80% of patients with confirmed FH [25]. Thus, both clinical and genetic diagnostic methods have significant limitations and lead to underestimation of the real prevalence of FH.

Another difficulty in estimating the true prevalence of FH is the heterogeneity of diagnostic criteria. The criteria used in different countries vary widely. A number of them are based on a point system, such as most widely used in Western countries - Danish Lipid Clinic Criteria. The Simon Broome criteria and the Japanese criteria for the diagnosis of FH are based mainly on such criteria's as clinical manifestations (hypercholesterolemia, tendon xanthomatosis) and a anamnesis of FH and/or early nascence atherosclerosis-associated cardiovascular disease. Such systems as MEDPED take in consideration only cholesterol levels and family history. The described variability of the criteria creates great difficulties in analyzing the results of studies from different countries and consequently including different ethnic cohorts. In addition, the criteria developed so far have been mainly focused on Western countries and therefore cannot be absolutely valid for another ethnic groups. Also, as data from new studies become available, there is a continuous process of revision of diagnostic criteria. For example, in 2020, scientists from Kanazawa University, Japan, conducted a study, according to the results of which, the threshold values of Achilles tendon thickness, after which it can be talked about a probable FH, were changed, the new interval is 7-9 mm (previously more than 9 mm) [18].

The existing problems of underestimating the racial and ethnic prevalence of FH have a number of significant socioeconomic implications. In particular, inequalities in cardiovascular risk evaluation in different ethnic groups; inequalities in access to approved statin therapy, as well as to new lipid-lowering drugs, inefficient allocation of available limited resources (medicines, equipment, human resources), especially in low- and middle-income countries. These facts in turn lead to progressive growth of atherosclerosis-associated cardiovascular diseases and, as a consequence, to increased disability and mortality of working-age adults.

The underestimation of racial and ethnic characteristics of FH is due to several factors, one of which is the so-called "structural racism in medicine" - unequal/ disproportionate involvement of representatives of different ethnic groups in clinical trials [52]. This factor leads to a lower representation of different ethnic groups, especially smaller ethnic groups in large-scale studies and, as a result, a lack of epidemiological data on these groups. In addition, a significant proportion of clinical trials are conducted in high-income countries, given the greater opportunities for their implementation and the a priori assumed reliability of the data obtained, which automatically excludes huge population cohorts from the analysis.

Obtaining reliable data on ethnic and racial differentiation of the prevalence of familial forms of hypercholesterolemia has a number of significant advantages. It is expected to increase the understanding of the pathogenesis of hypercholesterolemia and the burden of this pathology in non-European individuals, strengthen preventive medicine approaches, implement a system of screening, including cascade screening, optimize resource allocation and, as a consequence, improve the survival and quality of life of such patients.

Limitations and Future directions

It is important to take into account the many limitations of this systematic review when evaluating the results. First, the diagnostic standards and procedures applied in the included research vary significantly from one another. This variability makes direct comparisons more difficult and could result in disparities in the reported prevalence of FH across various racial and ethnic groups. Furthermore, the majority of the research included in this review were carried out in high-income nations, which might not fairly represent the world's population, especially in low- and middle-income nations where there is a dearth of information or nonexistence about the incidence of FH. The generalizability of the results is restricted by the absence of data from continents including Africa, South America, and portions of Asia. Additionally, the degree to which genetic testing is relied upon varies greatly throughout studies, and access to this type of testing is frequently restricted by economic and geographic reasons, which may result in underdiagnoses in less affluent areas. Last but not least, because homozygous variants are rarer and there are less studies on them, the review mostly concentrates on heterozygous types of FH.

Expanding research efforts to underrepresented regions, particularly low- and middle-income countries, is crucial to obtaining a more accurate global prevalence of FH. Additionally, future studies should focus not only on heterozygous FH but also on the homozygous forms to better understand the full spectrum of the disease. Standardizing diagnostic criteria and methodologies can help in early identification and management of the condition. All of the gaps in this review should be addressed in future research to provide a more comprehensive understanding of the prevalence of FH across different ethnic and racial groups globally. Overcoming the logistical and financial obstacles in these areas would require cooperation between global research institutes and regional healthcare providers. Lastly, earlier identification and treatment can be made possible by raising public and healthcare professionals' knowledge of FH, which will eventually improve patient outcomes.

Conclusion

To date, FH remains a disease that is underdiagnosed in a timely manner. Data from various studies agree on the overall prevalence of heterozygous forms in the range of 1: 192-303. At the same time, there are significant differences in estimates of the prevalence of FH in Asian, Hispanic, and Negroid populations. Moreover, the data differ with respect to both overall prevalence and patient cohorts. In some populations, such as the Africans, and Lebanese Christians, French Canadians and Gulf region population, where the "founder effect" is strong and the tradition of closely related marriages persists, there is a high incidence of both hetero- and homozygous forms. However, accurate statistics are not available everywhere. Regions such as Central Asian countries remain a white spot on the global map of FH prevalence. Consequently, epidemiological studies with maximum geographical coverage and ensuring equal inclusion of representatives of different ethnic groups are required.

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Community Based Cross-Sectional Study to Assess the Health Problems and Quality of Life Among Migrant Construction Workers in Chennai

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Abstract

Background: Although migrants often have less access to medical care, migrants are more likely to experience physical and mental health problems. As a result, the following goals guided the conduct of this study: to characterize the health issues faced by migrant workers in Chennai's construction industry, to ascertain their quality of life, and to evaluate their tendency to seek medical attention.

Methods: This cross-sectional study was carried out in Chennai's construction sites using community participants. The study included migrant laborers from across the state who work on construction sites for more than a year, both men and women over the age of 18. The research was carried out in 2023 between March and April. Convenient sampling was done, and 400 people were considered the sample size. Data were gathered using a pretested, structured Validated Questionnaire.

Results: The study showed that 13% had respiratory disease, 5.1% had acute febrile illness and 5.1 % had gastrointestinal disease. About 13% of the respondents went to nearby medical shop when they have any medical problems. About 62.0% of the participants had poor quality of life. Education (P=0.042), duration of working hours (P=0.034) and tobacco use (0.032) were found to be significantly associated with quality of life.

Keywords: occupational health, health problems, migrant construction workers, quality of life, health seeking

Introduction

Urbanization has been a growing trend in Indian society. India's urbanization rate increased from 27.81% in 2001 to 31.16% in 2011, according to the 2011 Census [1]. The two main drivers of migration are debt and destitution. India's states differ substantially in terms of their level of development; states like Kerala, Tamil Nadu, Gujarat, and Maharashtra have advanced further than states like Uttar Pradesh, Bihar, Jharkhand, and Chhattisgarh. Roughly one-third of India's labor force consists of migrant workers, who endure social isolation and restricted access to basic amenities such as water, sanitation, healthcare, and education, in addition to long hours and meager pay [2, 3].

The delivery of healthcare was also disrupted by internal displacement brought on by political unrest or migration due to trafficking. One of the oldest sectors in India is the construction industry, which employs a sizable number of people from low socioeconomic backgrounds [4-6]. Chennai, the capital city of Tamilnadu is experiencing a rise in the need for laborers. This is a result of the rapidly expanding fields of information technology, housing, trade, industrialization, metro rail construction and software development [7]. Amidst the city's towering buildings, thousands of migrant construction workers reside in makeshift sheds and tents by the side of the road. They either remain by the side of the road or on a building site/basement. The sheds lack electricity,

running water, sanitary facilities, ventilation, and safety features. [7] The employees frequently have a variety of illnesses. Frequent illnesses are caused by unclean water, unclean surroundings, and fly and mosquito-infested living areas.[5] The children frequently experience cholera, malnourishment, colds, and coughs brought on by breathing in paint fumes and dust and cement particles. Children are frequently seen on construction sites playing in the work areas and causing minor mishaps.[5]

Even though migrants are a significant population that is more likely to contract STIs or the HIV virus, there are not enough readily available services related to sexual health available for them.[7] Research from all over the world, including India, has shown that migrants use health services at a lower rate than the urban local population. This may be the result of a number of things, including cultural beliefs, socio-demographic status, women's autonomy, economic conditions, physical and financial accessibility, and disease pattern and health service issues, understaffing medical facilities and the marginalization of immigrant communities in general practice and primary care. Even though healthcare services are concentrated in cities, poor access to healthcare is caused by unpaid sick leave and financial insecurity [8–10].

The concept of quality of life, or QoL, is used to assess the level of wellbeing in a variety of vulnerable populations, such as migrants and refugees. [11–13] As "Individuals'" perception of their place in life in relation to their goals, standards, expectations, and concerns, as well as the culture and value systems in which they live, is how the World Health Organization (WHO) defined quality of life. It is a wide term that is highly impacted by a person's level of independence, mental health, physical well-being, social connections, and proximity to notable environmental features.[14] This concept brought to light the fundamental subjectivity of life's quality.[15] Prior empirical research indicated that psychological disorders and subsequent physical illness were strongly predicted by perceived quality of life. [16,17]. Therefore, understanding and improving health, wellbeing, and mental health within a variety of vulnerable groups—including migrants from rural to urban areas who moved in search of employment and a better life—requires research on quality of life (QoL) within a population.

Most of the migrant workers suffer from multiple health problems which makes them more susceptible to frequent sickness absenteism and loss of income. They need to be treated appropriately and get back to their work at the earliest, which mainly depends on their health seeking behaviour.

Studying QoL among a population is an essential step to understand and improve health status, well-being, and mental health among various vulnerable populations, such as rural-to-urban migrants who moved for seeking jobs and a better life. Hence this study was conducted with the following objectives:

1. To outline the health issues that Chennai's migrant construction workers face.

2. To assess the quality of life of migrant laborers employed in construction in Chennai

3. To evaluate the health-seeking habits of Chennai's migrant construction labor force

Methodology

This cross-sectional study was carried out in Chennai's construction sites using community participants. The study included migrant laborers from across the state who work on construction sites for more than a year, both men and women over the age of 18. Workers from other countries who declined to take part in the study were not included. The research was carried out in 2023 between March and April.

Sampling and sample size: Men's overall quality of life (QoL) was found to be 55.9, with a standard deviation (SD) of 3.7, in a study that was conducted in Bengaluru18. 400 was the sample size determined with a relative precision of 10% using the formulas 4 (SD)2/d2. The study participants were chosen using convenient sampling method until the required sample size was attained.

Ethical Concerns: Before the study began, approval from the institutional ethics committee, Government Medical College, Omandurar Government Estate, was secured. (IEC approval number **88/ IEC/ GOMC/ 22)**. We obtained informed consent from the participants. Privacy was guaranteed.

Research aid: arranged and verified beforehand A validated questionnaire was created in English, translated into the local language of the migrants by a professional scholar, and then translated back into English to guarantee linguistic validity. semi-structured survey comprising

1. a basic demographic profile and inquiries about potential health risks at work.

2. The WHOQOLBREF scale's14 standard questionnaire format was used to evaluate QoL. This instrument comprises 26 questions divided into four domains: environmental health (Domain 4), social relationships (Domain 3), psychological health (Domain 2), and physical health (Domain 1). A Likert scale with five points is used to rate each of these domains. In accordance with WHO guidelines, single item values were added to generate 25 raw scores for each domain. This resulted in a score that ranged from 0 to 100, with 100 representing the highest value and 0 representing the lowest. Each domain's mean score as well as the overall score were determined.

Statistical analysis: Using the Statistical Package for Social Sciences (SPSS) version 21.0, statistical analysis was carried out on all of the collected data that had been coded and entered into an Excel data sheet. Descriptive statistics like percentages and mean with standard deviation were used. Comparison of mean QOL with general characteristics of the patient was done using unpaired t test, if there are two categories and ANOVA was use if there were more than 2 categories. P value of less than 0.05 was taken as statistically significant.

Results

There were 400 workers total; 380 (or 95%) were men and 20 (or 5%) were women. 385 people (96.4%) were in the 15–45 age range. The workers' average age was 26.25 ± 8.49 years. 324 (81%) of the workers were married; 232 (58%) were Hindus, and 88 (22%) were Muslims. Overall, 228 people (57%) lacked literacy, compared to 96 people (24%) who had completed elementary, secondary, and higher secondary education, 40 people (10%), and 36 people (9%). 266 people (66.7%) in all belonged to a lower social class. Of the 400 workers who migrated, 168 (42%) came from Bihar, followed by 84 (21%) from Rajasthan, 60 (15%) from Jharkhand, 52 (13%) from Nepal, 12 (3%) from Odisha, and 24 (6%), from Assam (Table 1).

Workers suffering from past TB were 4(5.1%) and past malaria were 36(13%). Workers suffering with skin problems were 18(4.5%), respiratory problems like asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, pneumonia, and lung cancer were 52(13%), fever were 20 (5.1%), gastrointestinal system disease like Constipation, irritable bowel syndrome (IBS), nausea, gas, bloating and diarrhea were

20 (5.1%), musculoskeletal problems were 28 (7%).Workers hospitalisation< 1 were 27 (15%) and work place injury were 44 (11%). 4.5% workers had eye disease. In all, 192 (48%) of the workers consumed tobacco and 68 (6.9%) consumed alcohol (Table 2).

Table 3 shows that 44% workers went to nearby government hospital for health seeking behaviour and about 13% of the respondents went to nearby medical shop when they have any medical problems.

Table 1 Sociodemographic characteristics of the respondents

Parameters	Subcategory	Frequency	Percentage
Age group	< 15	4	0.1%
	15-45	384	96.4%
	46-60	11	3.1%
	>60	1	0.3%
Gender	Male	380	95%
	Female	20	5%
Marital status	Married	324	81%
	Unmarried	76	19%
Religion	Hinduism	232	58%
	Muslim	88	22%
	Christianity	60	15%
	Sikhism	8	2%
	Jainism	12	3%
Education	Uneducated	228	57%
	Primary	96	24%
	Secondary	40	10%
	Higher secondary	36	9%
Place of origin	Bihar	168	42%
	Rajasthan	84	21%
	Jharkhand	60	15%
	Nepal	52	13%
	Odisha	12	3%
	Assam	24	6%
Duration of working hours	4 to 6 hours	12	3%
	6 to 8 hours	20	5%
	8 to 12 hours	36	12%
	More than 12 hours	36	80%

Table 2 Medical history of the respondents

Medical history	Frequency	Percentage
1. Tobacco	192	48%
2. Alcohol	68	6.9%
3. Past tb	4	5.1%
4. Past malaria	36	13%
5. Hospitalisation < 1 year	27	15%
6. Fever	20	5.1%
7. Respiratory disease	52	13%
8. Skin disease	18	4.5%
9. Eye disease	18	4.5%
10. Gastrointestinal system disease	20	5.1%
11. Musculoskeletal problems	28	7%
12. Work place injury	44	11%

Table 3 Health seeking behaviour of the respondents

Parameters	Subcategories	Frequency	Percentage
Vaccination status of children	Fully vaccinated upto age	240	65%
	Not vaccinated up to age	160	35%
Health seeking behaviour	Nearby government hospital	176	44%
	Nearby PHC	172	43%
	Nearby medical shop	52	13%

Table 4 Quality of life of the participants

Quality of Life	Frequency	Percent
Good	152	38.0
Poor	248	62.0

The mean QOL score was 262.31 ± 45.12 . The QoL scores were further converted into categorical variable by obtaining the mean score and dividing the group into those who got a score above the mean and those below the mean. They were labeled as good and poor QoL.

About 62.0% of the participants had poor quality of life.

Table 5 Sociodemographic characteristics of the respondents

Parameters	Subcategory	Frequency	Percentage
Age group	< 15	246.21 ± 42.58	0.096
	15–45	282.19 ± 54.38	
	> 45	270.63 ± 32.91	
Gender	Male	267.80 ± 46.73	0.114
	Female	252.84 ± 41.29	
Marital status	Married	268.01 ± 36.83	0.126
	Unmarried	254.63 ± 64.20	
Religion	Hinduism	268.04 ± 35.09	0.256
	Muslim	253.19 ± 67.75	
	Christianism	289.10 ± 73.28	
	Sikhism	233.00 ± 88.12	
	Jainism	254.11 ± 65.20	
Education	Uneducated	212.45 ± 24.28	0.042
	Primary	235.10 ± 35.21	
	Secondary	245.10 ± 45.95	
	Higher secondary	293.01 ± 38.05	
Place of origin	Bihar	277.85 ± 56.19	0.296
	Rajasthan	263.47 ± 47.29	
	Jharkand	256.03 ± 39.49	
	Nepal	268.95 ± 73.04	
	Odisha	254.92 ± 59.64	
	Assam	253.04 ± 63.28	
Duration of working hours	4 to 6	256.78 ± 46.32	0.034
	6 to 8	286.10 ± 46.29	
	8 to 12	246.47 ± 56.21	
	More than 12	237.06 ± 64.47	
Tobacco use	Yes	236.05 ± 35.39	0.032
	No	289.26 ± 47.28	
Alcohol use	Yes	256.05 ± 41.29	0.083
	No	269.23 ± 54.38	

Table 5 shows that education (P=0.042), duration of working hours (P=0.034) and tobacco use (0.032) were found to be significantly associated with quality of life.

Discussion

Respiratory conditions accounted for the largest morbidity at the construction site (13%). Respiratory issues were reported in 4.86% of workers, according to Gurav et al. [19]. Given that the accommodations are located on campus, there may be a greater chance of dust exposure during and after working hours, contributing to the higher prevalence in this study.

5.4% of the workers at this construction site experienced musculoskeletal issues.

According to Mohopatra [20], 40% of workers experience musculoskeletal disorders that impact different joints and muscles, extending from the foot to the neck. Because most work is mechanized in this study, there is likely less manual labor involved, which contributes to the lower prevalence of musculoskeletal disorders.5.1% of the workers at this construction site had an acute febrile illness.

According to this survey, 11% of employees suffered an injury while on the job. The construction sector is notorious for having a high accident rate. Over 90% of mishaps can be avoided [21]. Temperature extremes raise the risk of accidents, according to Ramsay [22]. Accidents can occur due to a variety of factors, including age, sex, personal habits (like working while intoxicated), personality traits (like taking risks), and the physical and mental health of the worker. The prevalence of injuries was 25.42% in a study [23].

The engineering company's regular on-site safety induction training and growing reliance on mechanized work may be contributing factors to the low prevalence of the study. Skin disorders such as fungal infections, contact dermatitis, and eczematous rash affected 4.5% of the workforce. Cement and lime can cause dermatitis that is irritant. It is commonly known that chromate and cobalt-containing cement can cause allergic contact dermatitis [23].

Due to exposure to chemicals, parasites, or infectious agents at work and in their homes, 5.1% of the study's participants experienced gastrointestinal issues, including loose motions, abdominal pain, constipation, and appetite loss.

Of the workers, 48% reported smoking, which is less than the national prevalence of 57% according to the National Family Health Survey from 2005–2006 [24]. According to the National Household Survey on drug abuse, 6.9% of workers reported drinking alcohol, which is less than the 21% national estimate [25]. 44% of the workforce sought medical attention at the adjacent government hospital, while 43% visited the nearby primary health center. For 48% of workers, their quality of life was neither good nor bad.

In our study education (P=0.042), duration of working hours (P=0.034) and tobacco use (0.032) were found to be significantly associated with quality of life. In another study [18], It was observed that marital status, monthly income, type of work and shelter were significantly associated with environment domain of QoL and smoking had an influence on psychological domain of QoL. In our study, the mean QOL score was higher among married individuals but was not found to be significantly different. Our findings show that, having good education, having moderate work hours and avoiding tobacco are determinants of having good quality of life. The HRQoL (Health-Related Quality of Life) of migrant workers was influenced by factors such as age, monthly income, duration of residency, location of dwelling, and level of contentment with housing. The study found that there is a positive correlation between greater monthly income and higher quality of life (QoL) among migrant workers. This correlation is consistent with previous research that has shown higher QoL during periods of high economic levels [26, 27].

Three research [28-30] have shown that social support among migrant workers positively influences health behavior. Additionally, support systems such as medical services have been proven to enhance quality of life [23]. Furthermore, migrant workers were able to reduce their stress levels and enhance their quality of life by cultivating a sense of camaraderie and inclusion via the exchange of health-related interests and the establishment of a supportive community [29]. These findings are consistent with earlier research [31, 32] that have examined the connection between social support and quality of life across different populations. Specifically, these research have highlighted social support as a significant factor that affects the quality of life related to health. Social support not only enhances enjoyment and alleviates stress, but also enhances the quality of life (QoL) for migrant workers [33], hence improving their health-related quality of life (HRQoL). Hence, it is imperative to provide proactive assistance in order to enable migrant workers to establish self-help collectives, thereby improving their ability to manage stressful circumstances and cultivate good emotions.

The inability to test the construction workers for HIV was a limitation of this study. Furthermore, research on the use of personal protective equipment and its effect on preventing workplace injuries was not feasible.

It is imperative that behavior change communication be used to target lifestyle diseases like addiction and vector-borne diseases, as well as the use of personal protective equipment to prevent injuries. In order to diagnose infected patients early and ensure that they receive radical treatment under supervision at the construction site, active surveillance of fever cases should be prioritized.

Conclusions

Fever, respiratory disease, Skin disease, Eye disease, gastrointestinal system disease and musculoskeletal problems were the common illnesses present among the workers. Health seeking behaviour was poor among the respondents where about 35% of the respondents had not vaccinated their children upto age and about 13% of the respondents went to nearby medical shop when they have any medical problems. About three fifth of the respondents were having poor quality of life. Having good education, having moderate work hours and avoiding tobacco are determinants of having good quality of life.

Recommendations

The pattern of health issues among construction workers revealed by this study will help in the future development of worker-specific health promotion initiatives. Efforts should be made to improve their health seeking behaviour. Moderation of their working hours and behaviour change communication to avoid tobacco will improve their quality of life. Awareness should be created to them about the importance of education in improving the quality of life.

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Do Comorbidities and Body Mass Index Influence Shoulder Pain, Disability and Joint Range of Motion?

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Abstract

Aim: Shoulder diseases are believed to be associated with metabolic factors including diabetes and obesity. Our research aimed to determine how age-related comorbidities and rising body mass index (BMI) affected shoulder pain, disability, and joint range of motion (ROM).

Methods: The study included 137 individuals aged 20–80 who sought treatment for chronic shoulder pain at the physical medicine and rehabilitation outpatient clinic and, they were recorded for their demographics, BMI, comorbidities, pain duration, dominant shoulder, affected shoulder, history of treatment, joint ROM, visual analogue scale pain score, and shoulder pain and disability index score.

Results: The study found that the obese group had a high mean age (p=0.047) and substantially more common thyroid dysfunction (p=0.031). When individuals with and without diabetes mellitus (DM) were compared, it was observed that the DM group had significantly less ROM. Similarly, ROM was found to be considerably lower in the group with hypertension (HT) when a comparison was made for having or not having HT. In comparison of patients with or without hyperlipidemia (HL), the group with HL had significantly lower BMI compared to the group without HL (p=0.047). Upon comparing the groups with and without thyroid disease, it was discovered that the former had a considerably higher BMI (p=0.012).

Conclusion: We found that the two most prevalent disorders associated with shoulder pain, DM and HT, have a particularly positive influence on joint range of motion. We also observed a connection between thyroid problems and BMI. In the management of shoulder discomfort, managing comorbidities and BMI are crucial.

Keywords: diabetes; hypertension; joint range; obesity; shoulder pain.

Introduction

After knee pathology and spine pathology, shoulder pain stands as the third most prevalent musculoskeletal complaint [1].

Comorbidities of individuals with adhesive shoulder capsulitis had a substantial impact on pain and functioning [2].

According to epidemiological research, having a high body mass index (BMI) puts one at a considerable risk for developing a number of chronic diseases, including metabolic and musculoskeletal disorders [3,4].

Studies suggest that there is a relationship between shoulder disorders and metabolic factors such as obesity [5,6] and diabetes [6].

The release of leptin and other adiponectin from the shoulder joint has been reported in obese patients with shoulder pain, and the pro-inflammatory qualities of adiponectin have been proposed as a possible explanation for the association [7].

Shoulder disorders have been associated with interleukin (IL) -1 [13,14,15] and IL-6 and tumor necrosis factor (TNF) α [8-10].

Obesity promotes C-Reactive protein (CRP) production, mostly through circulating IL-6 levels [11].

There is research in the literature on the effect of obesity on patients undergoing shoulder arthroplasty [12,13], but only few investigations on patients with persistent shoulder pain who did not have surgery.

The research we conducted sought to investigate the effects of increased BMI and comorbidities, which are the problems of our age, on shoulder pain, disability and range of motion (ROM).

Materials and methods

The ethical committee of the local institute approved this study protocol through the institutional review board (date: 24.04.24 Decision no:AESH-BADEK-2024-318). The study also conforms to the principles set forth in the declaration of Helsinki. The study procedure was clarified to those who participated, and their written informed consent was collected in the manner mandated by the local institute's ethical committee.

This cross-sectional study included 137 patients aged 20-80 years who applied to the physical medicine and rehabilitation (PMR) outpatient clinic with chronic shoulder pain (pain duration of more than three months) [14].

History of trauma or surgery on the shoulder, pregnancy, malignancy, rheumatic diseases, cervical radiculopathy, brachial neuritis, complex regional pain syndrome and immunodeficiency were the exclusion criteria.

Demographic characteristics of the patients, BMI (kg/m2), comorbidities (diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), thyroid dysfunction, renal disease, valvular heart disease, arrhythmia, coronary heart disease, chronic obstructive pulmonary disease (COPD), asthma), pain duration, dominant shoulder and affected shoulder, previous treatment for shoulder pain, joint ROM, visual analogue scale (VAS) pain score and shoulder pain and disability index (SPADI) score were recorded.

A conventional 10-cm VAS was used to measure pain intensity; 0 represented "no pain," and 10 represented "unbearable pain" [15].

The SPADI, which consists of 5 items to assess pain and 8 items to assess disability, was used to assess the shoulder functional status (pain and disability). Higher scores indicate greater pain and disability. The score runs from 0% to 100% [16].

SPADI comprises a total score as well as subparameters for pain and activity limitation. There are five questions in the pain subparameter about shoulder pain in daily activities, and there are eight questions in the activity limitation subparameter about difficulty carrying out daily tasks. Patients rate their responses on a scale of 0 to 10, and the total of all response scores is divided by the total number of questions in each subparameter to obtain the value of that subparameter. Two subparameter scores are averaged to determine the total SPADI score. A high score denotes worsening shoulder function and more pain [17,18].

BMI was computed as body weight divided by height squared (kg/m2). There are three weight categories for participants: normal (18.5-24.9 kg/m2), overweight (25.0-29.9 kg/m2), and obese (>= 30.0 kg/m2) as defined by the World Health Organization (WHO) [19].

Statistical analysis

The SPSS for Windows 22.0 package was used for data analysis. The Shapiro Wilks test was utilized to determine whether continuous variables demonstrated a normal distribution. For continuous variables, descriptive statistics were shown as mean ± standard deviation; for nominal variables, they were shown as number of observations and (%). Using the Mann Whitney U test, the significance of the difference between the paired groups was examined with regard to all parameters and continuous variables. The Kruskal Wallis or Pearson's Chi-Square tests were used to assess nominal variables. When the Kruskal Wallis test was used, the results were given as median (min-max). When $p<0.05$, the results were deemed significant.

Results

The samples' mean age was 54.44 (SD 10.86). 68.4% were women and 30.8% were men. 16.5% were those who had jobs above shoulder level. 48.1% were primary school graduates. Demographic data are presented in Table 1.

Table 1 Demographic data

Variables		N=137
Age mean (SD)		54.20(10.72)
Gender n (%)	Female	95(69.3)
	Male	42 (30.7)
BMI mean (SD)		29.17 (4.82)
Symptom duration n (%)	3-6 months	57(41.6)
	6-12 months	26(19.0)
	>12 months	54(39.4)
Affected shoulder n (%)	Right	82(59.9)
	Left	55(40.1)
Dominant side n (%)	Right	131(95.6)
	Left	6(4.4)
Education level n(%)	Illiterate	15(10.9)
	Primary school	68(49.6)
	Middle school	7(5.1)
	High school	27(19.7)
	College	3(2.2)
	University	17(12.4)
Occupation n (%)	Heavy work above shoulder level	24 (17.5)
	No heavy work above shoulder level	113 (82.5)
Previous treatment received n (%)	Analgesic/NSAID	137(100)
	Injection	17(12.4)
	PMR	16(11.7)
Comorbidity n (%)	DM	28(20.4)
	HT	24(17.5)
	HL	18(13.1)
	Thyroid function disorder	16(11.7)
	Renal disease	3(2.2)
	Heart valve disease	3(2.2)
	Arrhythmia	1(0.7)
	COPD	1(0.7)
	Asthma	1(0.7)
VAS mean (SD)		6.99(1.6)
SPADI mean (SD)		66.09(16.94)
Abduction mean (SD)		157.66(26.43)
Adduction mean (SD)		35.25(10.27)
Internal rotation mean (SD)		67.62(24.18)
External rotation mean (SD)		71.67(23.05)
Flexion mean (SD)		159.56(24.55)
Extension mean (SD)		36.24(9.88)

BMI: Body mass index; NSAID: Nonsteroidal anti-inflammatory drugs; PMR: Physical medicine and rehabilitation; DM: Diabetes mellitus; HT: Hypertension; HL: Hyperlipidemia; COPD: Chronic obstructive pulmonary disease; VAS: Visual analogue scale; SPADI: Shoulder pain and disability index

The top 3 most common comorbidities were DM, HT and HL. Thyroid dysfunction was in the 4th place.

Patients were grouped according to BMI. They were divided into 3 groups: normal, overweight and obese. It was observed that the mean age of the obese group was high (p = 0.047). It was also seen that thyroid dysfunction was substantially greater in the obese group (p = 0.031). No significant difference was found between groups based on BMI in terms of symptom duration, abduction, adduction, internal rotation, external rotation, flexion and extension, VAS and SPADI (p values were 0.169, 0.581, 0.407, 0.358, 0.322, 0.696, 0.228, 0.832, 0.765 respectively). The results according to BMI are shown in Table 2.

Abduction, adduction, internal rotation, external rotation, flexion, and extension have been shown to be considerably lower in the DM group (p values were 0.000, 0.049, 0.000, 0.001, 0.001, 0.037, respectively) when the groups were split into those with and without DM. (Table 3).

Table 2 Comparison of groups according to BMI

Variables		Normal	Overweight	Obese	p
Age median (min-max)	52.5(28-74)	52.5(24-79)	57(39-75)	0.047#	
Gender n (%)	Female	19(63.3)	33(61.1)	43(81.1)	0.058*
	Male	11(36.7)	21(38.9)	10(18.9)	
Symptom duration n (%)	3-6 months	17 (56.7)	24 (44.4)	16 (30.2)	0.169*
	6-12 months	3(10)	11(20.4)	12(22.6)	
	>12 months	10(33.3)	19(35.2)	25(47.2)	
Affected shoulder n(%)	Right	20(66.7)	36(66.7)	26(49.1)	0.123*
	Left	10(33.3)	18(33.3)	27(50.9)	
Dominant side n(%)	Right	29(96.7)	50(92.6)	52(98.1)	0.359*
	Left	1(3.3)	4(7.4)	1(1.9)	
Education level n(%)	Illiterate	0(0)	5(9.3)	10(18.9)	0.423*
	Primary school	16(53.3)	26(48.1)	26(49.1)	
	Middle school	1(3.3)	3(5.6)	3(5.7)	
	High school	8(26.7)	11(20.4)	8(15.1)	
	College	0(0)	2(3.7)	1(1.9)	
	University	5(16.7)	7(13)	5(9.4)	
Occupation n(%)	Heavy work above shoulder level	8(26.7)	11(20.4)	5(9.4)	0.109*
	No heavy work above shoulder level	22 (73.3)	43 (79.6)	48(90.6)	
Previous treatment received n(%)	Analgesic	6(20)	9(16.7)	10(18.9)	0.920*
	NSAID	8 (26.7)	12 (22.2)	17 (32.1)	0.517*
	Injection	6(20)	7(13)	4(7.5)	0.252*
	PMR	5(16.7)	4(7.4)	7(13.2)	0.407*
Comorbidity n(%)	DM	5(16.7)	8(14.8)	15(28.3)	0.189*
	HT	4(13.3)	11(20.4)	9(17.0)	0.712*
	HL	7(23.3)	8(14.8)	3(5.7)	0.065*
	Thyroid function disorder	2(6.7)	3(5.6)	11(20.8)	0.031*
	Renal disease	0(0)	1(1.9)	2(3.8)	0.517*
	Heart valve disease	0(0)	0(0)	3(5.7)	0.088*
	Arrhythmia	0(0)	0(0)	1(1.9)	0.450*
	COPD	0(0)	0(0)	1(1.9)	0.450*
	Asthma	0(0)	0(0)	1(1.9)	0.450*
VAS median (min-max)		7.5(3-9)	7.5(2-10)	7(3-9)	0.832#
SPADI median (min-max)		69.2(26.9-100)	66.1(30-100)	71.5(37.6-90.7)	0.765#
Abduction median (min-max)		170(90-180)	160(60-180)	170(90-180)	0.581#
Adduction median (min-max)		45(20-45)	40(10-45)	30(10-45)	0.407#
Internal rotation median (min-max)		90(20-90)	70(10-90)	70(10-90)	0.358#
External rotation median (min-max)		90(20-90)	75(20-90)	80(20-90)	0.322#
Flexion median (min-max)		175(90-180)	160(90-180)	170(90-180)	0.696#
Extension median (min-max)		42.5(10-45)	40(10-45)	40(10-45)	0.228#

*:Pearson Chi-kare test #:Kruskal Wallis test

BMI: Body mass index; NSAID: Nonsteroidal anti-inflammatory drugs; PMR: Physical medicine and rehabilitation; DM: Diabetes mellitus; HT: Hypertension; HL: Hyperlipidemia; COPD: Chronic obstructive pulmonary disease; VAS: Visual analogue scale; SPADI: Shoulder pain and disability index

BMI, symptom duration, VAS, and SPADI did not significantly differ between individuals with and without DM (p values were 0.099, 0.186, 0.461, and 0.586, respectively) (Table 3).

The HT group showed considerably less abduction, adduction, flexion, extension, internal rotation, and exterior rotation (p values were 0.049, 0.015, 0.030, 0.011, 0.020,0.012 respectively) (Table 3).

When we compared those with and without HT, no significant difference was found in terms of BMI, symptom duration, VAS and SPADI (p values were 0.700, 0.703, 0.422, 0.251 respectively) (Table 3).

When we grouped them as those with or without HL, BMI was found to be significantly lower in the group with HL than in the group without HL (p =0.047) (Table 4).

No significant difference was found in the groups with and without HL in terms of symptom duration, abduction, adduction, internal rotation, external rotation, flexion and extension, VAS and SPADI (p values were 0.501,0.272,0.732, 0.816, 0.683, 0.668, 0.649, 0.580, 0.105 respectively) (Table 4).

When the groups with and without thyroid dysfunction were compared, BMI was found to be significantly higher in those with thyroid dysfunction (p=0.012) (Table 4).

No significant difference was found in the groups with and without thyroid dysfunction in terms of symptom duration, abduction, adduction, internal rotation, external rotation, flexion and extension, VAS and SPADI. (p values, 0.699, 0.580, 0.997, 0.881, 0.694, 0.576, 0.384, 0.388, 0.320, respectively) (Table 4).

Table 3 Comparison of groups according to DM and HT

Variables	w/ DM	w/o DM	p&	w/ HT	w/o HT	p&
BMI mean (SD)	30.35(4.53)	28.8(4.85)	0.099	29.95(5.19)	29.02(4.73)	0.700
Symptom duration n (%)						
3-6 months	8(28.6)	49(45)	0.186	9(37.5)	48(42.5)	0.703
6-12 months	7(25)	19(17.4)		5(20.8)	21(18.6)	
>12 months	13(46.4)	41(37.6)		10(41.7)	44(38.9)	
VAS mean (SD)	7.21(1.34)	6.9(1.65)	0.461	7.16(1.16)	6.92(1.59)	0.422
SPADI mean (SD)	67.7(15.8)	65.6(17.2)	0.586	69.6(16.8)	65.3(16.9)	0.251
Abduction mean (SD)	143.9(22.1)	161.1(26.3)	0.000	146.6(30.8)	160(24.9)	0.049
Adduction mean (SD)	31.78(10.5)	36.1(10.06)	0.049	30.2(11.3)	36.3(9.75)	0.015
Internal rotation mean (SD)	51.4(25.1)	71.8(22.19)	0.000	56.45(27.6)	70(22.8)	0.030
External rotation mean (SD)	58.75(24.6)	75(21.5)	0.001	60(24.8)	74.1(21.9)	0.011
Flexion mean (SD)	147.5(23.6)	162.6(23.9)	0.001	147.08(30.57)	162.2(22.3)	0.020
Extension mean (SD)	33.03(10.39)	37.06(9.62)	0.037	31.04(10.9)	37.3(9.3)	0.012

& :Mann Whitney u test
BMI: Body mass index; DM: Diabetes mellitus; HT: Hypertension; VAS: Visual analogue scale; SPADI: Shoulder pain and disability index

Table 4 Comparison of groups according to HL and thyroid dysfunction

Variables	w/ HL	w/o HL	p&	w/ TFT dysfunction	w/o TFT dysfunction	p&
BMI mean (SD)	27.4((3.7)	29.4(4.9)	0.047	32.1(5.35)	28.78(4.6)	0.012
Symptom duration n (%)						
3-6 months	6(33.3)	51(42.9)	0.501	7(43.8)	50(41.3)	0.699
6-12 months	4(22.2)	22(18.5)		1(6.3)	25(20.7)	
>12 months	8(44.4)	46(38.7)		8(50)	46(38)	
VAS mean (SD)	6.77(1.69)	7(1.59)	0.580	7.25(1.65)	6.93(1.59	0.388
SPADI mean (SD)	72.4(16.8)	65.1(16.8)	0.105	69.4(18.5)	65.6(16.7)	0.320
Abduction mean (SD)	155(22.8)	158(27)	0.272	161.8(21.36)	157.1(27.06)	0.580
Adduction mean (SD)	36.1(9.16)	35.1(10.4)	0.732	35.3(10.7)	35.2(10.2)	0.997
Internal mean (SD)rotation	66.1(24.9)	67.8(24.1)	0.816	67.5(23.7)	67.6(24.3)	0.881
External rotation mean (SD)	69.1(23.7)	72(23.03)	0.683	75.3(20.7)	71.1(23.3)	0.694
Flexion mean (SD)	161.6(23.070	159.2(24.8)	0.668	163.12(21.8)	159(24.9)	0.576
Extension mean (SD)	36.9(9.8)	159.2(24.8)	0.649	34.6(9.56)	36.4(9.9)	0.384

& :Mann Whitney u test
BMI: Body mass index; HL: Hyperlipidemia; TFT: Thyroid function tests; VAS: Visual analogue scale; SPADI: Shoulder pain and disability index

Discussion

We revealed that DM and HT, which are the two most common diseases accompanying shoulder pain, are especially effective on joint range of motion.

We found that the average age of our patients with chronic shoulder pain was 54.2 years. In one study, the median age of the patient group who received tipped shoulder injection for chronic shoulder pain was found to be 57. Again, in the same study, the number of women was found to be higher, as in ours. It seems that right shoulder involvement is more common, which is in line with our study [20].

In a study where HILT (high intensity laser therapy) was applied for chronic shoulder pain, unlike ours, the male rate was found to be higher. In the same study, the average BMI was found to be 24.55 and this value is within normal limits. In our study, we determined that the average BMI was above the ideal weight [21].

In the study by Cuce et al., BMI was determined as 29.3 in patients diagnosed with rotator cuff tear and they found the most common comorbidity to be HT. These results are similar to ours in terms of BMI, but we found the most common comorbidity to be DM [22].

In a study, they found that the most common disease accompanying chronic shoulder pain was HT. DM ranked 2nd. In our study, DM was ranked first, and HT was ranked second. In the same study, it was determined that a total of 37.8% had received physical therapy before and 8.5% had a history of surgery. We found that 10.9% of them received PMR and 12.9% had a history of injection. We accepted those with a surgical history as an exclusion criterion [23].

A statistically significant relationship was observed in one study between the increase in BMI and the pain intensity, SPADI scores and erythrocyte sedimentation rate (ESR) values. A statistically significant difference was observed between the obese group and the other groups, despite the fact that there was no statistically significant difference in any of the measures between the normal weight and overweight groups [24].

ESR and CRP values of our patients were within normal limits, but they were not evaluated as numerical values.

Weight-related variables, especially abdominal obesity, were linked to shoulder pain in either gender, according to research by Rechardt et al. Additionally, it has been demonstrated that persistent rotator cuff tendinitis is connected to abdominal obesity [14].

In type 1 diabetes, metabolic byproducts of non-enzymatic glycation accumulate in tendons [25].

Men's rotator cuff tendinitis and type 1 diabetes have been linked [14].

Men with type 2 diabetes were also shown to have a higher prevalence of rotator cuff tendinitis [14].

Buyuksireci et al. demonstrated in their study that being female and over 50 years old and having HbA1c levels between 5.7 and 6.4 increased the development of tendinosis susceptibility [26].

DM was shown to be the most common comorbid disease overall, despite the fact that our research was conducted without respect to gender.

In the study by Reid et al., in which they evaluated before and after arthroplasty, preoperative and postoperative pain was found to be worse in obese patients, but the magnitude of the change in pain scores after anatomical or reverse total shoulder arthroplasty was found to be similar to that in non-obese patients [27].

One study found no association of BMI with nonspecific shoulder pain [28].

Gandhi et al. examined levels of leptin, adiponectin, and resisting in synovial fluid (SF) samples. It was discovered that higher levels of SF leptin and adiponectin were correlated with greater pain. Functional outcome scores were not correlated with adipokine levels [7].

In the study evaluating shoulder arthroplasty patients, preoperative functional scores and quality of life of morbidly obese patients were found to be worse compared to other groups [29].

A correlation has been found between impaired shoulder function, obesity and high cholesterol [30].

We did not find a relationship between ROM, VAS, SPADI and HL or obesity.

Both preoperative and postoperative BMI have been reported to be inversely related to internal rotation in shoulder arthroplasty patients [31].

In individuals with breast cancer, lymphedema, postoperative immobility, and obesity have been shown to contribute to the development of adhesive capsulitis [32].

We did not detect any difference between groups based on BMI in terms of ROM.

One study suggested that thyroid autoimmunity in Hashimoto's disease may lead to an increase in thickness of shoulder tendons [33].

No significant difference was found in the groups with and without thyroid dysfunction in terms of symptom duration, ROM, VAS and SPADI in our study.

Conclusion

We found that DM and HT, which are the two most common diseases accompanying shoulder pain, are especially effective on joint range of motion. In addition, the group with obesity had a considerably greater mean age and thyroid dysfunction than the other groups. We conclude that weight control and treatment of comorbidities are important in patients experiencing pain in the shoulders. The significance of lifestyle and metabolic variables in shoulder disorders requires prospective investigations.

Pros and cons of research: The fact that this research examined a small number of patients cross-sectionally may be considered a limitation, but we strongly believe it is important in terms of drawing attention to the problem of our age, obesity and comorbidities, through shoulder pain.

Author Contributions: This research was conducted by Yasemin Tombak hence, conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article, critical revising and final approval were all carried out by the same author. The author has read and agreed to the published version of the manuscript.

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Statement of Ethics: The research was approved by the ethics committee of the local institute, Ankara Etlik City Hospital, Ankara, Turkey (date: 24.04.24 Decision no:AESH-BADEK-2024-318) and was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: The procedure of the study was explained to the participants and their written consent was obtained in the format required by the ethics committee of the aforementioned local institute.

Data Availability Statement: The author confirms that the data supporting the findings of this study are available within the article. The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

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Determinants of Health Behaviors Among University Students: Insights from a Cross-Sectional Study in the Karaganda Region

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Abstract

Aim: Many scholars highlight the insufficient commitment to a healthy lifestyle among student populations, often attributed to the challenges associated with academic transitions and social adjustments. Understanding the factors influencing student health behaviors is crucial for promoting well-being and fostering healthy lifestyles.

Methods: This study employed a cross-sectional analysis using primary data of 1327 students. The survey covered socio-economic factors and aspects of a healthy lifestyle among students from various universities in the Karaganda region, including Medical, Technical, and Humanitarian universities. Multiple logistic regression analysis was conducted to identify determinants influencing students' health behaviors.

Results: Demographic analysis revealed that surveyed students were primarily urban-born, enrolled in medical university programs, and predominantly lived with parents or relatives. Most students reported financial capacity for medical care and rated their social standing favorably. A significant proportion exhibited a normal BMI, with a notable prevalence of chronic diseases. While emergency care utilization varied, general practitioner visits were common, albeit less frequent among students with chronic conditions. Factors influencing health behaviors included educational program enrollment, socio-economic status, residential circumstances, gender, age, vaccination status. Understanding the complex interplay of factors influencing student health behaviors is essential for designing effective health promotion programs within universities.

Conclusion: This study provides valuable insights into the determinants of health behaviors among students, shedding light on areas for intervention and emphasizing the importance of fostering a healthy lifestyle for overall well-being and academic success.

Keywords: health behavior, students, Kazakhstan, health promotion

Introduction

Health encompasses more than just the absence of illness; it embodies complete physical, mental, and social well-being, as articulated by the World Health Organization in 1946. It stands as a paramount value in every individual's life, demanding protection and preservation. Not only does health hold significance at a societal level, serving as a barometer of collective well-being, but it also holds personal value, serving as a foundation for achieving life's aspirations [1, 2].

According to World Health Organization paradigm, health is shaped by various factors: socio-economic circumstances (50%), genetic predispositions (20%), environmental conditions (20%), and the level of healthcare access and quality (10%) [3, 4]. Consequently, health is heavily influenced by lifestyle choices. Thus, the field of valeology emerges with the goal of promoting and preserving health [5]. A pivotal

component of this endeavor is fostering a healthy lifestyle, which not only enhances personal well-being but also contributes to professional growth [6].

Despite its importance, many scholars highlight the insufficient commitment to a healthy lifestyle among student populations, who represent a vital segment of any nation's future [2]. This lack of commitment often stems from the challenges associated with transitioning to academic and professional pursuits and adapting to new social environments. The rigorous demands of academia frequently lead to unhealthy habits and compromised health due to time constraints [7-9].

A healthy lifestyle is multifaceted, encompassing behaviors that bolster physical, mental, and social well-being. It entails regular exercise, nutritious eating habits, abstaining from harmful substances like tobacco and alcohol, routine medical check-ups, and prioritizing mental health [10]. Aligned with national initiatives like the "Healthy Nation" project, healthcare policies increasingly prioritize the promotion of healthy lifestyles as a fundamental strategy [11].

Currently, addressing the health of students is a pressing research concern, given the escalating rates of health issues among young people. Despite their generally robust health, student life significantly influences health behaviors and habits [12-14]. Studies worldwide explore the myriad factors shaping students' adherence to healthy lifestyles [15]. For instance, Bronfenbrenner's ecological systems model underscores the impact of social, cultural, and political factors alongside individual experiences [16].

Research underscores divergent health behaviors across academic disciplines. While medical students typically prioritize health due to its professional relevance, students in humanities may exhibit contrasting habits, such as irregular eating or excessive alcohol consumption [17-19]. Notably, studies indicate variations in health consciousness among students of different specialties, with those in medical and biological fields demonstrating greater attentiveness compared to their peers in humanities or technical disciplines [20, 21]. However, students in technical fields often lack adequate valeological education, highlighting the imperative of studying their orientation toward health [22].

Understanding these disciplinary differences is crucial for designing effective health promotion programs within universities, making detailed research in this area indispensable. Thus, this study aims to analyze and evaluate student behavior concerning health across various universities and education programs, using the Karaganda region as a case study.

Materials and Methods

We conducted a cross-sectional, retrospective analysis using primary data. To examine students' health-related behaviors across different fields of study, we employed a survey method administered remotely through Google Forms. The questionnaire covered socio-economic factors like age, gender, education, place of residence, origin, financial and social status, as well as aspects of a healthy lifestyle such as physical activity, dietary habits, and substance use. Participation was voluntary and anonymous, involving students from various universities in Karaganda: Medical University (46% of respondents, referred to as "medical" henceforth), Technical University (26.8% of respondents, referred to as "technical"), and Humanitarian University (27.2% of respondents, referred to as "humanitarian").

Ethical approval for the study was obtained from the local Bioethics Commission at Karaganda Medical University. Karaganda was chosen due to its status as a major educational hub in Kazakhstan, attracting students from across the country. A total of 1327 students participated, comprising 666 first-year, 232 second-year, 232 third-year, 160 fourth-year, 35 fifth-year, and 1-6 year students. Among respondents, 64.2% were female and 35.8% were male. The majority (43.4%) fell within the 17–18 age bracket, followed by 19–20 years (31.9%), 21–23 years (11.6%), over 24 years (12%), with only 0.2% below 17 years. Data processing, descriptive analysis, and visualization were conducted using Microsoft Office Excel and R-Studio.

Multiple logistic regression analysis was employed to identify determinants influencing various aspects of students' health behavior, including tobacco use (including electronic cigarettes and vaping), alcohol consumption, healthy dietary patterns, and physical activity levels.

Results

The analysis of demographic data revealed that the surveyed students had an average age of 21 years. Regarding the demographic profile of the sample, the majority of participants were urban-born (61.9%, 821 individuals), enrolled in medical university programs (46%, 611 students), with an average age of 21.12±7.24 years (Table 1).

Table 1 Demographical description of the sample

Variables	Total		Male		Female	
	n	%	n	%	n	%
Area of origin						
Urban	821	61.87	289	60.84	532	62.44
Rural	506	38.13	186	39.16	320	24.11
Education field						
Health science	611	46.04	169	35.58	442	51.88
Technical science	355	26.75	253	53.26	102	11.97
Humanitarian sciences	361	27.20	53	11.16	308	36.15
Age (mean, sd)	21.12 (7.24)	19.03 (2.49)	22.29 (8.64)			

Among students, various living arrangements were observed, with a slight majority opting to reside with their parents or relatives (389 individuals, constituting 29.31% of the total). When examining living situations by gender, it was noted that women tended to prefer living in their own apartments (252 individuals, comprising 29.58% of the sample). Notably, a significant proportion of both maternal (529 individuals, accounting for 39.86%) and paternal figures (428 individuals, representing 32.25%) boasted higher education qualifications, predominantly holding bachelor's degrees. A substantial 85.61% of students reported having both parents present in their lives. Moreover, the vast majority of students (888 individuals, totaling 66.92%) asserted their ability to comfortably afford medical medications, while a comparable number (835 individuals, encompassing 62.92%) affirmed their financial capacity for necessary medical examinations. On average, students rated their social standing at 7.80±1.72 and their financial position at 7.21±1.76, utilizing a scale where 1 denoted a very low position and 10 signified a very high position.

As depicted in Table 3, the preponderance of students exhibits a body mass index (BMI) falling within the normal

Table 2 Socioeconomic information of the sample

Variables	Total		Male		Female	
	n	%	n	%	n	%
Living condition						
Dormitory	354	26.68	135	28.42	219	25.70
Apartment	341	25.69	89	18.74	252	29.58
Rent	243	18.31	83	17.47	160	18.78
Living with family	389	29.31	168	35.37	221	25.94
Mother's education						
Bachelor	529	39.86	195	41.05	334	39.20
Secondary	345	25.99	118	24.84	227	26.64
Professional	312	23.51	84	17.68	228	26.76
Master	131	9.87	71	14.95	60	7.04
PhD	10	0.75	7	1.47	3	0.35
Father's education						
Bachelor	428	32.25	164	34.53	264	30.99
Secondary	424	31.95	141	10.63	283	33.22
Professional	355	26.75	110	8.29	245	0.12
Master	69	5.19	36	2.71	33	3.87
PhD	10	0.75	7	0.53	3	0.35
Nuclear family						
Yes	1136	85.61	407	85.68	729	85.56
No	191	14.39	68	14.32	123	14.44
Ability to buy medication (financial)						
Easy	888	66.92	325	68.42	563	66.08
Very easy	219	16.50	64	4.82	155	18.19
Hard	208	15.67	80	6.03	128	15.02
Very hard	12	0.90	6	1.26	6	0.45
Ability to get medical examination (financial)						
Easy	835	62.92	298	62.74	537	63.03
Very easy	155	11.68	50	10.53	105	12.32
Hard	311	23.44	116	24.42	195	22.89
Very hard	26	1.96	11	2.32	15	1.76
Social status (mean, SD)	7.80 (1.72)		7.69 (1.69)		7.87 (1.76)	
Financial status	7.21 (1.76)		7.06 (1.76)		7.27 (1.75)	

range, constituting 842 respondents or 18% of the total. Among these individuals, 176 respondents, comprising 55% of all those with chronic conditions, report living with chronic diseases. Interestingly, while the sample includes the fewest obese students (41 individuals, representing 3.09% of the cohort), they account for 50% of the group afflicted with chronic illnesses. Overall, a significant 77.24% of all respondents have engaged in health-related information searches at some point. Furthermore, a striking 90% of students grappling with chronic diseases have pursued relevant health or healthcare-related information online at least once.

Approximately 44% of students reported no recollection of health issues necessitating activity restrictions. A vast majority (91.11%) have undergone all required vaccinations without hesitation. On average, students sought emergency medical attention 0.69±1.39 times within the past 24 months. Remarkably, those with chronic ailments sought emergency care significantly more frequently (1.06±1.19) than their healthier counterparts (0.57±1.49), with a statistically significant difference (p-value <0.001) observed.

Over the preceding 12 months, students predominantly visited general practitioners, averaging 1.68±2.33 visits. Interestingly, students with chronic conditions exhibited a statistically significant lower rate of general practitioner visits

Table 3 Health behavior and health-related data

Variables	Total		Chronic diseases (yes)		Chronic diseases (no)		p-value
	n	%	n	%	n	%	
BMI							
Underweight	159	12.74	44	13.75	115	11.42	0.001
Normal	842	63.45	176	55.00	666	66.14	
Overweight	152	11.45	48	15.00	104	10.33	
Obese	41	3.09	16	50.00	25	2.48	
Health-related information search							
Yes	1025	77.24	288	90.00	737	73.19	<0.001
No	302	22.76	32	10.00	270	26.81	
Activity limitation because of health problem							
No limitations	347	26.15	102	31.88	245	24.33	<0.001
No health problems	579	43.63	29	9.06	550	54.62	
Limited, but not too much	401	30.22	189	59.06	212	21.05	
Vaccination status							
Yes	1209	91.11	294	91.88	915	90.86	0.66
No	118	8.89	26	8.12	92	9.14	
Health self-assessment							
Very good	268	20.19	13	4.06	255	25.32	<0.001
Good	707	53.28	122	38.13	585	58.09	
Not bad but not good either	329	24.79	167	52.19	162	16.09	
Bad	21	1.58	17	5.31	4	0.39	
Very bad	2	0.15	1	0.31	1	0.09	
Number of emergency medical care received within 24 months (mean, SD)	0.69 (1.39)		1.06 (1.19)		0.57 (1.49)		<0.001
Number of visits to a family doctor within 12 months (mean, SD)	1.68 (2.33)		1.51 (2.44)		1.78 (2.27)		<0.001
Number of visits to a specialist doctor within 12 months (mean, SD)	1.01 (1.73)		0.87 (1.52)		1.09 (1.83)		<0.001
Number of hospitalizations within 12 months (mean, SD)	0.15 (0.71)		0.18 (0.82)		0.14 (0.65)		<0.001
Number of visits to day hospital during 12 months (mean, SD)	0.76 (1.89)		0.78 (2.20)		0.75 (1.69)		0.27
Number of study days missed due to health problems within 12 months (mean, SD)	3.58 (9.82)		2.61 (5.69)		4.12 (11.47)		<0.001

(1.51±2.44) compared to those without chronic ailments (1.78±2.27), with a p-value <0.001.

In terms of consultations with specialized medical professionals, students sought their expertise approximately once annually (1.68±2.33 visits). Hospitalization and day hospital visits among students were infrequent, averaging 0.15±0.71 and 0.76±1.89, respectively.

Students missed an average of 3.58±9.82 study days due to health concerns, with those lacking chronic conditions

exhibiting a higher rate of absenteeism (4.12±11.47 days), though not statistically significant.

In Figure 1, the frequency of tobacco smoking, alcohol consumption, healthy eating, and physical activity over a one-week span is illustrated. The overwhelming majority abstain from both alcohol consumption and tobacco smoking entirely, comprising 86.59% and 87.26% of respondents, respectively. Notably, none of the students reported consuming alcohol daily, while a minor proportion (5.05%) admitted to smoking daily. A significant portion of students (21.32%) adhere to a healthy dietary regimen daily, ensuring adequate intake of fresh fruits and vegetables. However, a notable fraction (6.71%) claim to never prioritize healthy eating. As for physical activity, approximately equal proportions of students engage in exercise daily, less than once a week, and never, accounting for 15.22%, 15.37%, and 16.05% of the cohort, respectively.

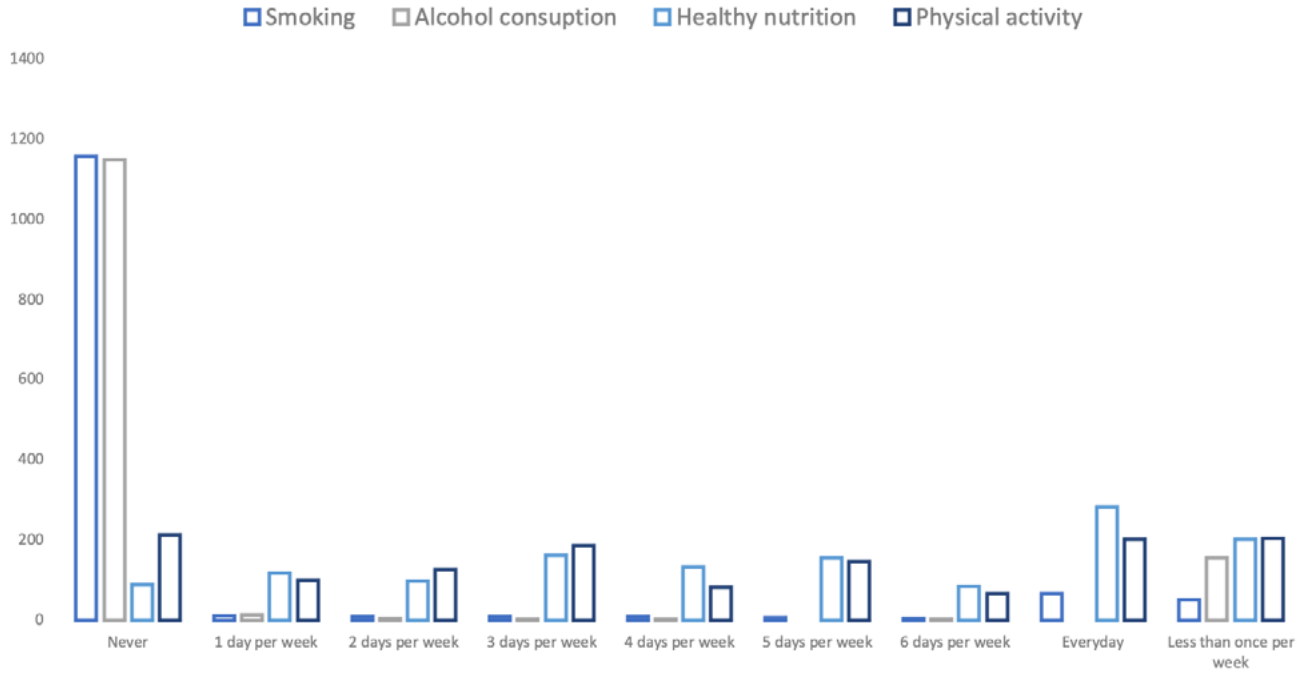

Figure 1 – Frequency of smoking, alcohol consumption, healthy nutrition and physical activity per week

Table 4 delineates factors influencing smoking, alcohol consumption, dietary habits, and physical activity among student participants. Notably, enrollment in a medical educational program emerges as a significant protective factor against smoking, reducing the odds by 53% (OR=0.47, p-value<0.01). Conversely, increased frequency of emergency medical care

Table 4 Factors influencing smoking, alcohol consumption, physical activity, healthy eating

Smoking				**Alcohol consumption**			
Covariate	**Odds Ratio**	**95% CI (2.5%, 97.5%)**	**p**	**Covariate**	**Odds Ratio**	**95% CI (2.5%, 97.5%)**	**p**
Health-related Education Program	0.47	-1.33, -0.19	<0.01	Health-related Education Program	0.36	-1.57, -0.46	<0.001
Number of emergency medical care received within 24 months	1.24	0.06, 0.35	<0.01	Engineering Education Program	0.55	-1.11, -0.09	0.02
Year of study	1.32	0.09, 0.46	<0.01	Urban area of origin	2.23	0.33, 1.29	<0.01
Male	5.04	1.08, 2.17	<0.001	Vaccination status	2.28	0.07, 1.66	0.04
Having chronic diseases	1.75	0.09, 1.02	0.02	Age	1.07	0.04, 0.09	<0.001
Drinking Alcohol more than once per week	26.15	2.81, 3.74	<0.001	Smoking	27.31	2.87, 3.76	<0.001
Healthy nutrition				*Physical activity*			
Health-related Education Program	0.41	-1.28, -0.49	<0.001	Health-related Education Program	0.45	-1.16, -0.45	<0.001
Living in dormitory	0.59	-0.94, -0.13	<0.01	Health information searching	1.93	0.32, 0.99	<0.001
Living in rent apartment	0.57	-0.96, -0.11	<0.01	Number of visits to a specialist doctor within 12 months	1.10	0.01, 0.19	0.04
Number of visits to a specialist doctor within 12 months	1.12	0.01, 0.22	0.04	Healthy nutrition	9.51	1.96, 2.55	<0.001
Challenges in acquiring medications stemming from financial constraints	0.17	-3.12, -0.06	<0.01				
Male	0.65	-0.78, -0.09	<0.01				
Self-assessment of health as good	4.69	0.38, 2.69	<0.01				
Physical active more than once per week	9.76	1.98, 2.58	<0.001				

within 24 months, higher academic year, male gender, presence of chronic diseases, and frequent alcohol intake (more than once per week) elevate the likelihood of smoking among students.

Moreover, gender disparities are pronounced, with male students exhibiting a 5.04-fold higher likelihood of smoking compared to their female counterparts (p-value<0.001). Similarly, frequent alcohol consumption (more than once per week) escalates the odds of smoking by 26.15 times (p-value<0.001) in this cohort.

Medical and technical educational programs demonstrate protective effects against alcohol consumption, reducing the odds by 64% (OR=0.36, p-value<0.001) and 45% (OR=0.55, p-value<0.05), respectively. Conversely, urban residence status heightens the probability of alcohol use by 123% (OR=2.23, p-value<0.01) compared to rural counterparts. Additionally, smoking significantly amplifies the odds of alcohol consumption among students by 27.31 times (p-value<0.001).

Furthermore, male students residing in dormitories or rented apartments, enrolled in medical programs, and lacking financial resources for medication procurement exhibit notably poorer dietary habits compared to their peers. Conversely, engaging in physical activity more than once a week and self-assessing one's health positively enhance the likelihood of healthy eating behaviors among students, by 9.76 times (p-value<0.001) and 4.69 times (p-value<0.01), respectively.

Discussion

The problem of preserving and strengthening the health of students lies not only in the intrinsic value of health, but also in the socio-economic status [23]. A student's social background, including income level, access to resources and support, and social circle, can have a significant influence on the choice of healthy or unhealthy behavioral habits [24, 25]. Research shows that students from families with a high level of socio-economic status among their parents have greater access to housing, food, education, health care and various social services than students with a low level of socio-economic status among their parents [26-28]. Because these services increase students' self-esteem and self-confidence, which in turn promotes a healthy lifestyle [29, 30]. The relationship between having both parents and college students' health behaviors is an important topic of public health research. Students raised by both parents may exhibit varying levels of healthy and unhealthy behaviors, which may have an impact on their physical and mental well-being. Research shows that students who grow up in dual-parent families often have more stable social and economic conditions, which can lead to healthier habits and lifestyles [31, 32]. Support from loved ones plays an important role in developing a healthy lifestyle among students. In today's society, where stress, pressure and temptation play a huge role, support from friends, family and partners can be key to achieving health and well-being. It is important to recognize that students who feel supported in their efforts to maintain a healthy lifestyle are more likely to make good decisions and engage in healthy habits, which in turn improves their overall well-being and academic success [33, 34]. Housing conditions play a significant role in shaping students' health behavior. Dormitories, rented housing, owning a home, and living with parents can all impact students' physical, emotional, and psychological well-being. Various studies have been conducted where it was found that students living separately from their parents in rented apartments have negative health behavior due to the relative freedom of action and lack of control. Students living in dormitories and living with their parents have relatively the same health behavior [35,36]. Adequate self-assessment of students' own health influences the preservation and improvement of their health status [37, 38]. Numerous studies indicate that the presence of health problems in family members, such as the risk of developing chronic diseases, dietary imbalances or low physical activity, has a significant impact on the health behavior of students [39, 40]. Health literacy is one of the most important determinants of health [41], which is associated with the social aspects of health [42-45] and represents a set of cognitive and social skills that determine the motivation and ability of people to seek, understand and use information for health promoting and maintaining good health [46-48]. Health literacy profoundly influences health behavior by equipping individuals with the ability to comprehend and utilize health information, thereby enhancing decision-making and health management. Conversely, low health literacy is associated with adverse health outcomes due to misunderstandings of medical instructions and difficulties in navigating the healthcare system.

A healthy lifestyle encompasses a multifaceted approach that includes maintaining a balanced diet, engaging in regular physical exercise, and eliminating harmful habits such as smoking and excessive alcohol consumption. Additionally, it involves consuming sweets in moderation, sustaining an active lifestyle, and prioritizing mental and psychological well-being. One of the core tenets of a healthy lifestyle is proper, balanced nutrition, which serves a crucial preventative function in mitigating the risk and progression of numerous chronic diseases. [49, 50]. According to WHO recommendations, vegetables and fruits should be present in the human diet every day, as they are sources of fiber, vitamins and minerals [51, 52]. One of the leading elements of educational processes is optimal physical activity. The level of physical fitness and the dynamics of somatic health are closely related to physical education [53, 54]. According to the recommendations of the World Health Organization, the norm for weekly physical activity of students is aerobic physical activity 2-3 times a week [55, 56]. One of the main aspects of a healthy lifestyle is avoiding alcohol and smoking. Such bad habits pose serious threats to a person's physical and mental health, and also increase the risk of developing many diseases, the transience of life and the deterioration of its quality. Scientists from all over the world conduct many studies confirming the harmful effects of alcohol and smoking on the human body. Impaired functioning of the cardiovascular system, the development of cancer, liver health problems and other complications are often associated with alcohol consumption. Student health researchers V.A. Medic and A.M. Osipov note that alcohol consumption has become a tradition among students and has persisted for decades. Students steeped in this tradition distort their perceptions of public opinion regarding problems associated with alcohol use [57-59]. In contemporary society, smoking is one of the most prevalent detrimental habits among students. This behavior not only jeopardizes the physical health of young individuals but also exerts a negative influence on their professional and personal growth. Tobacco smoking often signifies underlying issues in the social adaptation of students, indicating potential difficulties in coping with stress, peer pressure, and other social challenges. The habit of smoking substantially elevates the risk of dysfunction in multiple body systems, including the nervous, cardiovascular, endocrine, and immune systems. Moreover, it adversely affects other organs and systems within the body, leading to a broad spectrum of

health complications. This multifaceted impact underscores the critical need for targeted interventions and preventive measures to address smoking among students, thereby safeguarding their overall well-being and future potential [59, 60].

Conclusion

In conclusion, our analysis sheds light on various aspects of student health behavior and its determinants. Our findings underscore the multifaceted nature of student health, highlighting the interplay between individual characteristics, socio-economic factors, and environmental influences. By identifying key determinants of health behaviors, our study offers valuable insights for devising targeted interventions aimed at promoting student well-being and fostering healthier lifestyles.

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‘Patterns’ of COVID-19 Coronavirus Infection in Pregnant Women in Physician Practice

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Abstract

Objectives: Evaluation of the Effectiveness of Developed Algorithms for Managing Pregnant Women and Assessing Severity Using the WHO ABCDE Approach During COVID-19 Among Practicing Physicians

Material and methods: To evaluate the effectiveness of the algorithm for managing pregnant women and assessing severity using the WHO ABCDE approach during COVID-19, we analyzed 102 medical records of pregnant patients with COVID-19 who received treatment in infectious disease hospitals and perinatal centers in the city of Shymkent from January to April 2022.

Results: Diagnostic errors were made in 22.5% of the sample before the training on the developed algorithms. Following the training sessions, the error rate decreased by 7.8%. Physicians identified errors in the following diagnoses: influenza – 10.8% (11 cases), acute intestinal infections – 4.9% (5 cases), acute cerebrovascular accident, measles, and atypical pneumonia – 1.9% (2 cases each), and Kawasaki disease – 0.9% (1 case). After the training, the incidence of the diagnosis of "Influenza" decreased by 4.9% and "Acute intestinal infections" by 3%.

Our findings revealed that the percentage of diagnostic errors (underdiagnosis) significantly dropped from 41.2±6.9% (n=51) to 11.6%±4.9 ($p<0.01$) (n=43), representing a reduction of more than 3.6 times. The analysis of diagnostic errors related to the underdiagnosis of COVID-19 and the implementation of the algorithm for the management and severity assessment based on the WHO ABCDE approach led to a more than 3.6-fold decrease in cases of delayed diagnosis.

Conclusions: The analysis of diagnostic errors related to the underdiagnosis of COVID-19 and the implementation of the management and severity assessment algorithm based on the WHO ABCDE approach led to a more than 3.6-fold reduction in the number of delayed diagnoses.

Keywords: COVID-19, pregnancy, mistakes, SARS-Cov-2.

Introduction

On March 11, 2020, the WHO declared the COVID-19 outbreak a pandemic, and two days later, it announced that Europe had become the epicenter [1]. The number of cases without epidemiological links to explain the source of virus transmission was increasing. In the second half of March, the infection rapidly spread across European countries, while the number of cases in the United States surged [2]. On March 24, the WHO warned that the US was becoming the new epicenter [1]. By early 2022, data collected by the NWSS were considered an important independent source of information on the spread of SARS-CoV-2 in the US. As of May 23, 2024, more than 775 million cases of the disease had been registered worldwide, with over 7 million confirmed deaths, making the COVID-19 pandemic one of the deadliest in history [1].

From 2019 to 2023, there were six waves of COVID-19 globally. The first wave was recorded in December 2019. The peak of the second wave occurred in the spring of 2020. The third wave happened in June-July 2020. It is important to note that the seasonality of COVID-19 and influenza are not identical. November 2021 marked the fourth wave. The fifth wave occurred in January-February 2022. The final sixth wave was registered in August 2022 [1].

As of 2022, according to the Committee on Sanitary and Epidemiological Control of Shymkent, Kazakhstan, 1,394,287 cases of the disease were confirmed. Across the country, 1,379,442 people

recovered, and there were 13,069 deaths [3].

The COVID-19 incidence rate in December 2023 was 57.89 cases per 100,000 population. In Shymkent, it was 34.88 cases per 100,000 population [3].

From 2020 to 2023, Shymkent registered a total of 38,149 cases, of which 1,646 were pregnant women: 537 cases in 2020, 892 cases in 2021, and 217 cases in 2022 [1].The progression of the disease caused by the SARS-CoV-2 virus is directly dependent on the entry of the virus into host cells after binding to angiotensin-converting enzyme 2 (ACE2). ACE2 replicates on cell membranes and tropen in the placenta throughout pregnancy. This phenomenon is a possible etiology of predisposition of pregnant women to COVID-19 [4]. Reduced immune reactivity and other physiological changes during gestation cause an increased susceptibility to respiratory diseases and severe pneumonia in pregnant women, which can lead to hospitalization in intensive care units and mechanical ventilation [5]. A lightning-fast development of a critical condition is possible against the background of a fairly stable course of the disease in pregnant women with coronavirus infection COVID-19 [5].

Materials and methods

We have implemented the "Severity Assessment of COVID-19 in Pregnant Women Using the WHO ABCDE Approach" at the Municipal Infectious Diseases Hospital and the City Maternity Hospital in Shymkent as of October 15, 2021 (Appendix A). The management algorithms for pregnant women with COVID-19 and the severity assessment using the WHO ABCDE approach were integrated into the mandatory training program "Management and Early Diagnosis of Pregnant Women with COVID-19" for infectious disease specialists and obstetricians-gynecologists in Shymkent and the Turkestan region. This included institutions such as the Municipal Infectious Diseases Hospital, Regional Perinatal Center No. 2, and the City Maternity Hospital, with training conducted both in-person and online (Appendix A). Furthermore, these algorithms were incorporated into the infectious disease curriculum for 4th and 5th-year students and residents in "Infectious Diseases," "Obstetrics and Gynecology," and "General Practice" at the South Kazakhstan Medical Academy starting from November 2022.

Over seven months, 57 physicians from Shymkent and the Turkestan region, 15 residents specializing in "Infectious Diseases" and "Obstetrics and Gynecology," and 89 students from the South Kazakhstan Medical Academy underwent training.

To evaluate the effectiveness of the management algorithms and severity assessment using the WHO ABCDE approach for COVID-19 in pregnant women, we analyzed 102 medical histories of pregnant patients with COVID-19 treated in infectious disease hospitals and perinatal centers in Shymkent from January to April 2022.

Statistical Analysis

The normality of the distribution was checked using the Kolmogorov-Smirnov test with the Lilliefors correction. Since all data showed a normal distribution, the mean and standard deviation were subsequently used. Categorical variables are presented as absolute numbers, percentages, and frequencies. A p-value of <0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics 26.0.

Ethics

The study was approved by the Local Bioethical Committee of JSC "SKMA" (date: 03/16/2021). Written informed consent for publication was obtained from the patients or their legal representatives.

Results

To reduce the incidence of COVID-19 among pregnant women and prevent fatalities, we developed a step-by-step management algorithm for pregnant women with COVID-19 (Appendix A). This algorithm is based on the Clinical Protocol for the Diagnosis and Treatment of "COVID-19 in Pregnant Women, Women in Labor, and Postpartum Women" from March 4, 2022. The algorithm outlines management strategies for pregnant women with asymptomatic, mild, moderate, severe, and extremely severe COVID-19. Patients with symptoms such as fever, general weakness, malaise, loss of appetite, and cough (dry or with small amounts of difficult-to-expectorate sputum) receive outpatient treatment.

According to the algorithm, outpatient observation is provided for the following categories: pregnant women with asymptomatic COVID-19, pregnant women, and postpartum women with mild COVID-19, and pregnant women discharged from the hospital after recovering from COVID-19.

We recommend hospitalization for pregnant women with severe and extremely severe COVID-19. Physicians adhering to the algorithm can timely adjust the management sequence for pregnant women with COVID-19 during gestation.

Our next development was the severity assessment of COVID-19 using the WHO ABCDE approach (Appendix G). The ABCDE algorithm is an effective method for assessing the condition of critically ill patients. The steps of the ABCDE algorithm aim to identify and immediately correct life-threatening conditions. Progression to the next step in the ABCDE algorithm is possible only after correcting life-threatening conditions at the current step. This method is used for a systematic approach to each patient, enabling early recognition of life-threatening conditions.

According to our development, the initial assessment (A-airway) of the patient's condition is based on consciousness, positioning, and resting SpO2. The next parameter assessed for severity was breathing (B-breathing). Severe and extremely severe cases are identified by the presence of shortness of breath with minimal exertion or at rest, a respiratory rate of 30 breaths per minute or more, SpO2 <90%, and CT signs of pneumonia with typically >50% lung involvement.

The third step in severity assessment is circulation (C-circulation). Circulation is assessed using heart rate (60-80 beats/min for mild, 90-120 for moderate, over 120 beats/min for severe and extremely severe cases), skin color (pale pink for mild, pale pink, pale, hyperemic, cyanotic for moderate, pale, hyperemic, cyanotic for severe and extremely severe cases), and peripheral perfusion (less than 3 seconds for mild, 3-5 seconds for moderate, more than 5 seconds for severe and extremely severe cases). Neurological status (D-Disability) is assessed using consciousness and AVPU/GCS scores. External factors (E-Exposure) are determined by the presence of temperature, symptoms, and Doppler metrics.

To evaluate the effectiveness of the management algorithm and severity assessment using the WHO ABCDE approach for COVID-19 in pregnant women, we analyzed 51 medical histories of pregnant patients with COVID-19 treated in

infectious disease hospitals and perinatal centers in Shymkent from January to April 2022. We found that the percentage of diagnostic errors (underdiagnosis) significantly decreased from 41.2±6.9% (n=51) to 11.6±4.9% (p<0.01) (n=43), a reduction of more than 3.6 times. Physicians made diagnostic errors in 5 cases: 2 cases of incorrect diagnosis of respiratory failure (4.7%) and 1 case each (2.3%) of incorrect anticoagulant therapy, hemorrhagic complications, and ARDS (Figure 1).

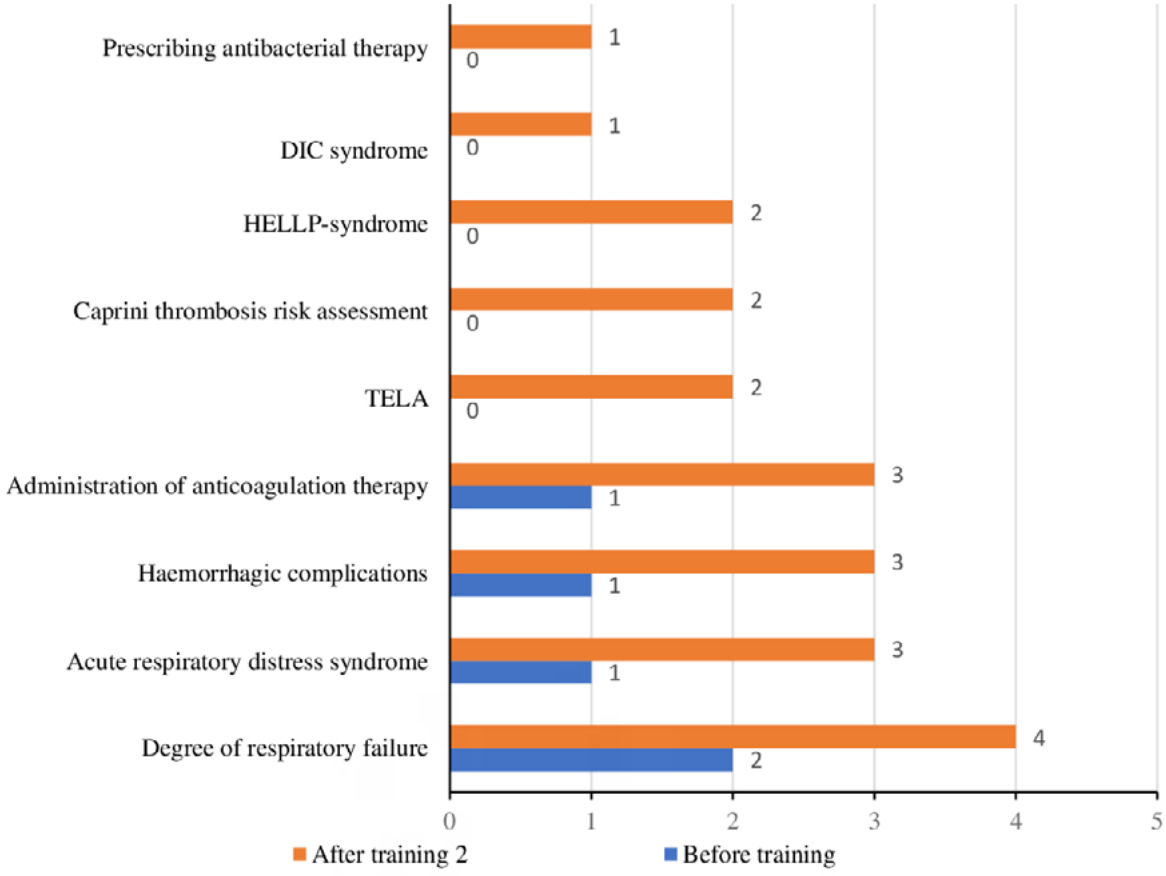

Figure 1 – Effectiveness of the Implementation of the WHO ABCDE Approach for the Management and Severity Assessment of COVID-19

Table 1 Effectiveness of misdiagnoses before and after the development training

Mistaken diagnoses	Before training n=102		After training n=102	
	Abs	%	Abs	%
Influenza	11	10,8	6	5,9
Acute gastrointestinal infections	5	4,9	2	1,9
Acute cerebrovascular disorder	1	0,9	0	0
Kawasaki disease	1	0,9	0	0
Measles	2	1,9	1	0,9
Atypical pneumonia	2	1,9	1	0,9

Note: The number of cases is shown in parentheses.

To examine the effectiveness of misdiagnoses before and after the development training, 102 case histories of pregnant women with coronavirus infection were studied. Table 1 shows the spectrum of misdiagnoses made by physicians before and after the trainings. Misdiagnosis errors were made in 22, 5% of the sample before the developmental trainings. Further, there was a decrease of 7, 8% after the trainings. Physicians made errors in the following diagnoses: influenza-10.8% (11), acute intestinal infections-4.9% (5), acute cerebral circulatory disorder, measles and SARS-1.9% (2), acute cerebral circulatory disorder and Kawasaki disease-0.9% (1). After development trainings among doctors, there is a decrease in the diagnosis of 'Influenza' by 4.9%, 'Acute intestinal infections' by 3%.

Discussion

The defects in the diagnosis of COVID-19 coronavirus infection and erroneous diagnoses described by us are consistent with the data of other authors. Thus, Khateeb J et al with co-authors in their work note that special difficulties in the diagnosis of viral diseases are noted in the initial period of the disease, flowing fever, myalgia, catarrhal syndrome [6,7]. The authors emphasise that in all cases of differential diagnosis first of all it is necessary to exclude acute neurological diseases and intestinal infections, respiratory diseases.

In our study, physicians before development training made a 10.8% error in the diagnosis of 'Influenza'. According to the protocol 'Coronavirus infection COVID-19 in pregnant, labouring and delivery women' the exclusion criteria for this diagnosis are marked catarrhal syndrome, scleritis, rhinorrhoea, tracheitis, relative lymphocytosis, negative PCR assay for SARS-Cov-2 [8-11]. The catarrhal period of measles is characterised by acute onset and fever, which is similar to coronavirus infection. At the same time, the criteria for excluding measles are a pronounced catarrhal syndrome, scleritis, conjunctivitis followed by a staged rash, Belsky-Filatov-Koplik spots and a

negative ELISA result. The picture of 'acute abdomen' may resemble nausea, vomiting, abdominal pain.

The authors of the article stress the importance of a properly collected epidemiological history in the differential diagnosis of COVID-19 coronavirus infection with other diseases [12,13].

Van den Berg P et al. in their work also emphasises that the use of standard case definition during the admission of patients with catarrhal syndrome allows to identify a patient with coronavirus infection in the first days of the disease, to isolate him in time and to start the necessary treatment [14].

The described clinical cases clearly demonstrate that health care providers need to be wary of patients with comorbidities during pregnancy [15,16]. This leads to hypodiagnosis of coronavirus infection, treatment at home or not infrequent hospitalisation of patients initially in somatic wards. This significantly increases the risks of transmission in family foci and non-core hospitalisations [17-21]. Worldwide, it is essential that physicians and medical staff from various specialities are vigilant, have up-to-date knowledge and apply modern diagnostic methods, algorithm of management tactics to reduce the likelihood of diagnostic errors when COVID-19 coronavirus infection is detected [21-24].

Recruitment of pregnant women with COVID-19 during the pandemic has been rapid, which is one of the strengths of the study. However, the study was conducted in only one city, which was the limitation. In the future, we plan to conduct research in other cities. Another limitation was that this study is single centre, which does not provide extended results. It should be noted that the sample size was relatively small.

Conclusion

Thus, the analysis of diagnostic errors associated with hypodiagnosis of COVID-19 coronavirus infection and the introduction of the algorithm of management tactics and severity assessment based on the WHO ABCDE approach resulted in a 3.6-fold decrease in the number of delayed diagnoses and helped to avoid delays in initiating the necessary pathogenetic and etiotropic therapy.

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A Clinical Case of Successful Surgical Correction of Tetralogy of Fallot by Using the Right Atrial Appendage as a Neopulmonary Valve

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Abstract

Tetralogy of Fallot (TOF) is a common cardiac malformation characterized by reduced pulmonary circulation. Long-term preservation of neopulmonary bicuspid valve function is crucial in paediatric cardiac surgery. In 2019, Iranian cardiac surgeon Amirghofran A. introduced a novel method of forming a neopulmonary valve from the right atrial appendage. Despite numerous previous attempts to preserve the pulmonary valve using both autologous and foreign tissue, results were often disappointing. The usage of the right atrial appendage as a bicuspid valve in the pulmonary position offers an alternative method for correcting TOF with a deformed, hypoplastic, or aplastic pulmonary valve. However, further follow-up is required to obtain more reliable data.

Keywords: Tetralogy of Fallot, neopulmonary valve, right atrium appendage, right ventricular outflow tract.

Introduction

Tetralogy of Fallot (TOF) is a common cardiac malformation characterized by reduced pulmonary circulation. For many years, the surgical technique for correcting TOF remained unchanged. Despite numerous attempts to improve the technique, many proposed methods were not practical. In 2019, Iranian cardiac surgeon Amirghofran A. introduced a novel method of forming a neopulmonary valve from the right atrial appendage. This method serves as an alternative option for hypoplasia and aplasia of the pulmonary valve annulus. One notable benefit is the use of autologous valves, which may facilitate growth and potentially reduce the need for repeat interventions in children with pulmonary valve insufficiency and restenosis. [3-5]. In our opinion, one of the most promising techniques is the use of the right atrium appendage as a neopulmonary valve. More than 100 operations using this technique have been performed with good results, but it has not been used in post-Soviet countries.

Clinical case

The first successful surgical correction of Tetralogy of Fallot by using the appendage of the right atrium as a neopulmonary valve was performed in the paediatric cardiac surgery department of JSC NSMC (November 22, 2023) for the first time in Kazakhstan. Patient A., aged 11 months, was admitted with complaints of dyspnoea, sweating when feeding and crying, and lividity of the nasolabial triangle when restless. The examination according to echocardiography revealed the following: CHD. Tetralogy of Fallot: subaortic defect of the interventricular septum. Moderate tricuspid regurgitation. Aortic dextroposition of 50%. Combined pulmonary artery stenosis with trunk and branch hypoplasia. Gradient on the RV/PA is 85/42 mmHg. Condition after endovascular stenting of the RVOT. Hypertrophy of right ventricle myocardium. Ejection fraction (EF) is 75%. Left ventricular hypertrophy is present. Cardiac computed tomography angiography (CTA) with contrast reveals a functioning stent of the right ventricular outflow tract (RVOT), aortic dextraposition up to 50%,

RVOT obstruction, and myocardial hypertrophy of the right ventricle. Dilatation of all heart chambers is also observed. CTA findings are unremarkable, with no evidence of coronary artery obstruction, stenosis, or anomalies.

The duration of the operation was five hours, with a total time of artificial circulation of 178 minutes. The aortic clamping time was 78 minutes, with a blood loss of 15 ml. During the operation, the hypoplastic pulmonary artery trunk was opened and placed on holders. At the time of the revision, the pulmonary valve was bicuspid, the pulmonary leaflets were fused with the stent, and the leaflets were thickened and restricted in movement. Gradually, the valve leaflets were detached from the stent. Further, during revision through the pulmonary valve annulus, the bougie №5 was passed, which did not correspond to the calculated z-score parameters (z score parameters should be within 8-10 mm). It was therefore decided to cut the annulus and implant a neopulmonary valve formed from the appendage of the right atrium.

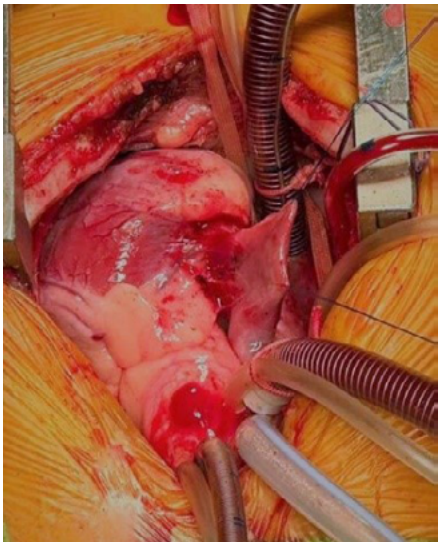

Figure 1 – Harvesting and preparation of the right atrial appendage (photo was taken during the operation)

Following the closure of the ventricular septal defect with a Gore-Tex patch and the excision of the right ventricular outflow tract by cutting hypertrophied and fibrotic tissues of the RVOT, the rudimentary pulmonary valve leaflets were excised, and a neopulmonary valve derived from the right atrium appendage was implanted in the location of the native pulmonary valve annulus (Fig. 1, 2, 3). The right atrium appendage was prepared in advance: The edges of the right atrium appendage were secured in position using prolene 5/0-10 thread. The rough portion of the right atrial appendage was then detached from the trabecular muscles. On the opposite edge of the appendage, a scalpel incision was made to correspond to the estimated diameter of the pulmonary valve annulus. Subsequently, the lateral edges of the neobicuspid valve were sutured in the projection of the pulmonary artery trunk. The next step involved suturing the lower edge of the leaflet of the neobicuspid valve to the pulmonary valve annulus. Subsequently, dilating plasty of the pulmonary artery trunk and right ventricular outflow tract was performed using xenopericardium. Additionally, the second leaflet of the neopulmonary valve was sutured to the xenopericardium in the region of the pulmonary valve annulus to preserve the haemodynamic geometry of the valve, thus avoiding neobicuspid valve deformation and insufficiency. On the control transoesophageal echocardiogram, the gradient on the RV/PA

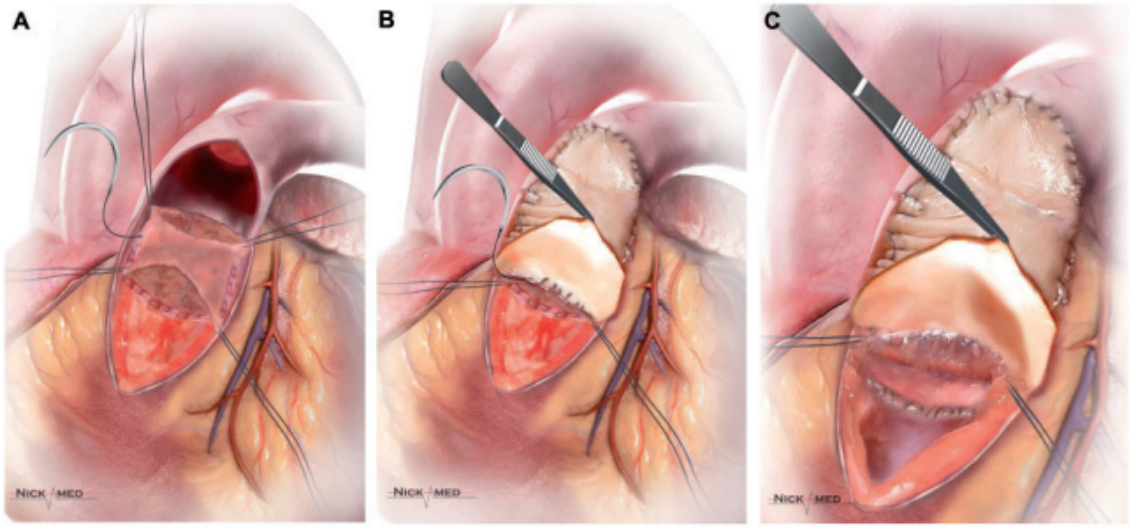

Figure 2 – Suturing the right atrial appendage valve in the place. (A) The posterior part of the annulus and then the two lateral edges are sutured to make the left and right commissures. (B) The bovine transannular patch covers the pulmonary arteriotomy, and the anterior annulus is sutured. (C) The final shape of the bicuspid right atrial appendage valve (the figure was taken from [1])

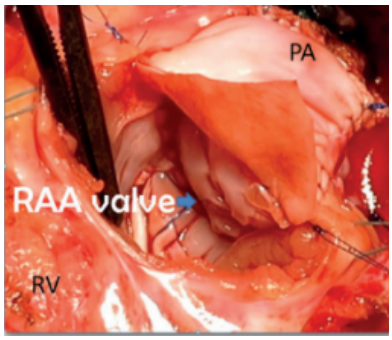

Figure 3 – Bicuspid neovalve (the figure was taken from [1]

was 14 mmHg. There was no pulmonary valve regurgitation, and only light tricuspid regurgitation was observed. The VSD patch was found to be closed tightly. The patient's ejection fraction was 50%. The patient was admitted to the intensive care unit (ICU) for two days and was extubated on the first day after surgery without complications. The patient was discharged after ten days. On the control echocardiogram before discharge, the gradient in the right ventricle to pulmonary artery (RV/PA) was 22 mmHg. There was a mild pulmonary regurgitation. The right part of the heart was dynamic with a reduction. The left

ventricular pumping and contractile function was satisfactory, with an ejection fraction (EF) of 60%.

Discussion

In the long term, the preservation of neopulmonary bicuspid valve function in Tetralogy of Fallot has a key value in paediatric cardiac surgery. Previously, numerous attempts have been made to preserve the pulmonary valve using both autologous and foreign tissue, but the results have been disappointing. Given that the use of the biological or mechanical valve in small children is not possible, this technique represents a potential solution to this problem. It is now possible to preserve the pulmonary valve for a long period of time, thanks to our colleagues from Iran, led by Amirghofran A. However, it should be noted that this method is not a panacea for all patients and that careful selection is required. In the case of an abnormally short, fused or absent appendage of the right atrium, this method is not applicable. In preparing the right atrial appendage (RAA), the following criteria must be met: the width of the RAA should be equal to half the circumference of the design annulus, and the height should be equal to the diameter of the design annulus. Additionally, the inner part of the right atrial appendage should be thoroughly cleaned of rough trabeculae. Given that the tissue of the right atrial appendage is autologous, anticoagulant therapy is not required. This surgical technique has no age restrictions and can be used in both 15-day-old babies and 57-year-old patients with tetralogy of Fallot. It is not limited to this condition and can also be applied in the treatment of pulmonary atresia type 1, Nikaidoh operation, common arterial trunk, and absent pulmonary valve syndrome [9-13].

Conclusion

It can be concluded that the use of the right atrial appendage as a bicuspid valve in the pulmonary position represents an alternative method for the correction of Tetralogy of Fallot with deformed, hypoplastic and aplasic pulmonary valve. The new technique is safe, easy to perform and the first successful results in Kazakhstan are promising. Given that the right atrial appendage is autologous tissue, there is a possibility of valve growth, which could represent a new branch in the improvement of surgical tactics in Tetralogy of Fallot. However, further follow-up is required to obtain data that are more reliable.

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Giant Frontal Sinus Osteoma Presenting as Abducens Nerve Palsy with a Local Granulomatous Inflammation: Case Report with a Literature Review

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Abstract

Osteoma is one of the rare benign bone tumors and often presented asymptomatic. The current article will present a case report of giant frontal sinus osteoma and successful surgical treatment. The size of the tumor described is remarkable and among the largest currently reported. In a discussion section, we try to provide the helpful groundwork for this disease's etiology and describe the surgical approach performed. The purpose of this study is to present the clinical symptoms, radiological findings, and surgical indications of a giant frontal sinus osteoma with an orbital cavity expansion and secondary VI cranial nerve palsy. Moreover, histological findings of the tumor showed granulomatous inflammation and tumor-infiltrating lymphocytes with single multinucleated giant cells, leading us to provide additional antibacterial treatment and perform an osteoplastic operation 6 months later.

Keywords: giant osteoma, local inflammation, osteoplasty.

Introduction

Osteomas are benign, slow-growing bone tumors primarily developed from the paranasal and craniofacial sinuses [1]. Only 0.03% of primary bone tumors that have undergone biopsy are osteomas [2]. Osteomas in the orbit can present with various symptoms depending on their location and size. Due to the limited space within the orbit, the growth of an osteoma can lead to compression of the surrounding structures, resulting in symptoms such as proptosis (bulging of the eye), restricted eye movement, diplopia (double vision), and visual disturbances. Furthermore, in cases where the osteoma extends into the sinus cavity, it can cause sinus congestion, facial pain, and deformity [1, 3]. Recurrence is quite rare: according to one literature analysis that gathered data on 477 cases, recurrence or persistent residual disease of osteoma only occurred in 12 (2.5%) individuals with a mean follow-up of 29.7 months [3]. Primary bony tumors of the skull make up only 1% of all bone tumors, and only 25% of all craniofacial osteomas were found in the orbit, whereas 17% implicated the frontal bone [4]. The cranial osteomas can be classified into skull base osteomas, skull vault osteomas, dural osteomas, and intraparenchymal osteomas, with skull base osteomas being the most prevalent among these groups [5]. Orbital extensions may be present in frontal sinus osteomas. The cranial nerves III, IV, and VI, the ciliary ganglion, and the ophthalmic sympathetic nerve fibers are all located within the relatively small cavity of the orbit, which is a bony pyramid with an approximate volume of 30cm3 [6]. An orbital extension that exceeds 50% of the orbit may cause irreparable harm, such as permanent vision loss [6]. In this case, the right eye's proptosis and VI cranial nerve palsy were caused by the protrusion of the tumor into the orbital region. This case report aims to provide a successful case of resected frontal sinus osteoma that expanded to the roof and lateral walls of the orbit.

Case description

A 31-year-old female with a history of minor head trauma at the age of 2 and hepatitis B arrived at the National Center of Neurosurgery in April 2023 with bulging in her right eye. For the previous five years, the patient had been suffering from terrible widespread headaches. Other complaints included swelling, pain in the right eye, and proptosis that progressed during the last 2 years. During the neurological examination, VI CN palsy was observed in the form of horizontal diplopia.

The CT and MRI scans were performed, revealing signs of the osteoid formation of the right frontal sinus and the orbit's destruction. Periorbital edema and proptosis (Figure 1 C, D) were seen, and a performed MRI revealed that the right eye was dislocated to approximately 6.6 mm from orbit and the signs of a tumor formation in the intracranial space.

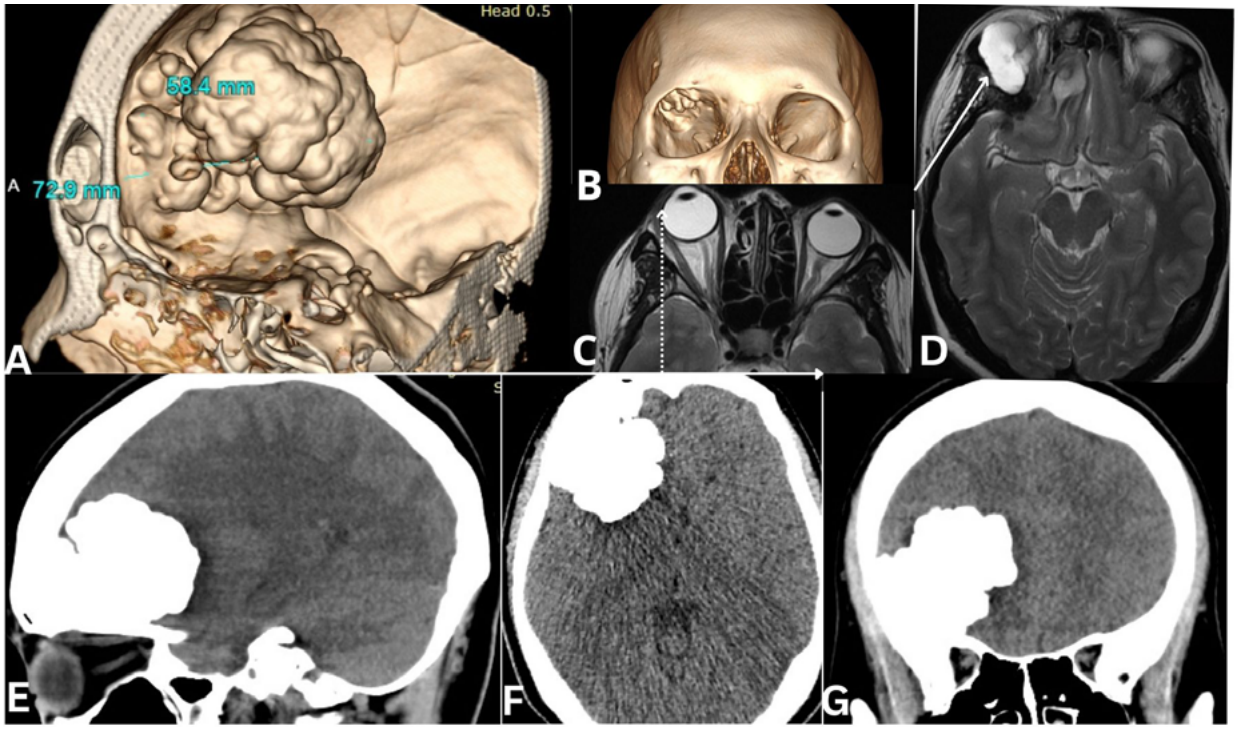

Figure 1 – Initial presentation of the patient's osteoma with measurements on CT (Figure 1a); figure 1B demonstrates invasion to the frontal bone; the dotted line on figure 1C demonstrates the proptosis, and an arrow on figure 1 D shows sign of granulomatous inflammation. There are signs of the orbital destruction (Figure 1E, 1F, 1G)

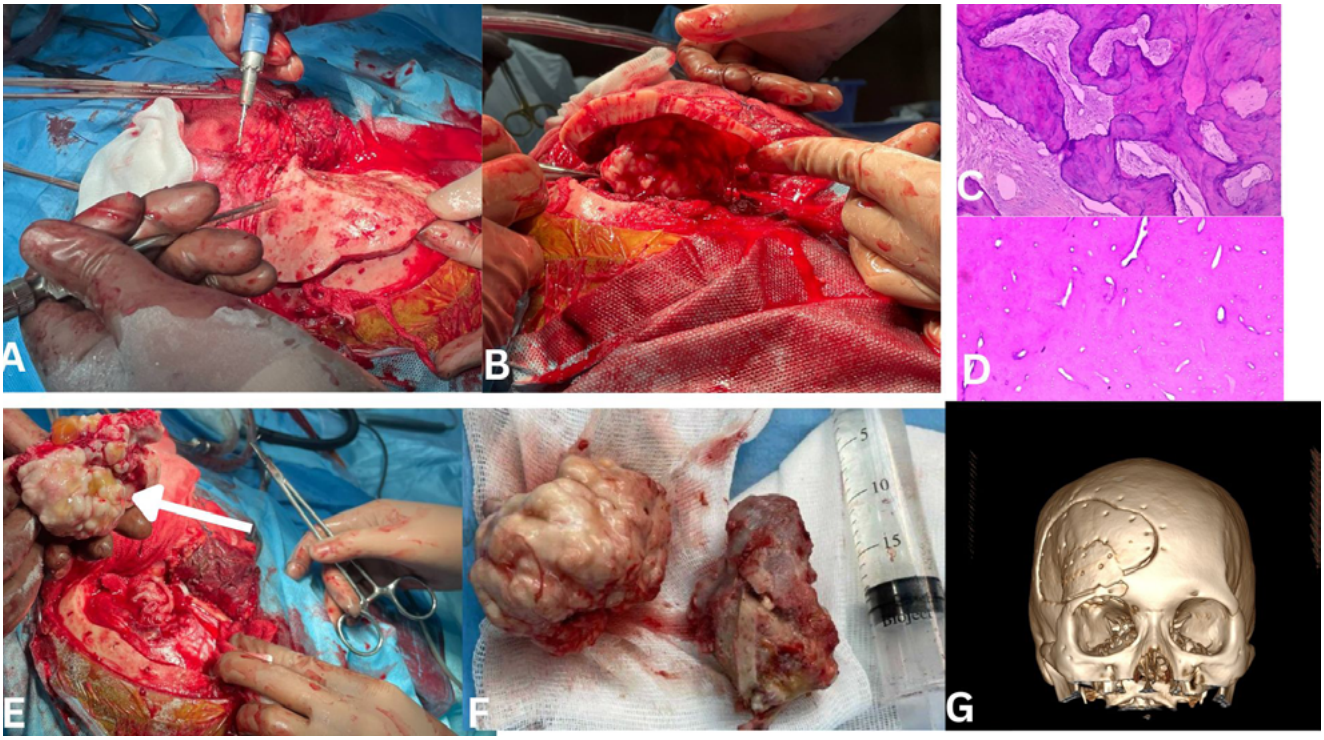

Figure 2 – Intraoperative images demonstrating modified frontotemporal approach (figure 2A), bone elevation with detachment of the osteoma from dura mater by a dissector (figure 2B), removed part of the bone with the tumor attached to it, local inflammatory reaction on the surface of the osteoma was seen as yellow membranous part (arrow on the figure 2E), post-resection images of the tumor (figure 2F). Histopathological evaluation with H&E stain revealed the presence of osteocytes within the dense bone matrix, with minimal fibrous stroma noted (C, D). Figure 2G demonstrates a post-operative CT demonstrated total removal with osteoplasty.

A firm mass was palpated at the angle of the right orbit. A cerebral computed tomography (CT) scan (Fig. 1E, F, G) showed a polypoid and irregularly shaped solid bony mass with well-defined borders and intracavitary growths occupying the anterior part of the frontal sinus and extending toward the intracranial surface of the orbit with thinning of the lateral wall of the frontal sinus and causing 7 mm frontal lobe displacement to the left. CT of the head revealed a 7 cm × 5.8 cm × 6 cm well-defined, lobulated, irregularly shaped solids with bony consistency markedly radio-dense lesion arising from the frontal bone and right frontal sinus. The tumor had extended upward to the right orbit's superior wall, showing significant intracranial extension. The mass had displaced the globe and the orbital soft tissues inferiorly and laterally. Supra-lateral part of the orbit had T2 hyperintensity signals (Fig. 2 D), indicating an inflammatory process beneath.

The mass was responsible for irreducible and non-pulsatile right eye proptosis of 6.6 mm with superolateral globe displacement and lateral rectus paralysis. Visual acuity and sharpness were preserved.

Operation

The patient has undergone a pterional craniotomy (Figure 2A, B), where the orbital roof destruction and dura erosion were distinguished. The right frontal sinus was opened and sealed with a hemostatic sponge after thorough washing with chlorhexidine. Further work on the olfactory fossa provided a layered reconstruction of anterior cranial fossa defects with periosteum. Another muscle flap was superimposed on top to ensure total sealing. The optic nerve was intact. The dura mater was sutured using an artificial dura. The part of the frontal lobe was partially removed and modified, the osteoma adjacent to the bone was cut out completely, and the remaining bone, not damaged by the tumor, was left in place. Because of the signs of the inflammation during the operation (fig 2E), the decision was made to perform an osteoplastic operation 6 months later. The compressed part of the right frontal lobe had parenchymal bleeding and signs of necrosis; the bleeding was consequently removed with hemostasis provided. The operation was performed without complication, and the patient regained consciousness after a few hours.

Histology

The tumor, divided into two parts, exhibited features of osteoma on histological examination. The first part consisted mainly of mature lamellar bone tissue, while the second part showed infiltration by lymphocytes and multinucleated cells resembling foreign bodies. The tumor mass, discovered post-surgery, had a polypoid shape with a smooth white and yellow surface composed of mature lamellar bone tissue with osteons (fig 2 C, D). Microscopic analysis revealed active granulomatous inflammation, and the case was classified as an ivory-type osteoma based on these findings. It is recognized that the granulomatous inflammation surrounding a tumor is an indication of the host immune system reacting to the tumor.

Postoperative Course and Follow-Up

The clinical course following the craniotomy was successful: headaches were gone, and proptosis regressed consequently. The patient was able to regain lateral gaze ocular movements. No neurological deficits were identified. There were no incisional infections, meningitis symptoms, or neurological deficits. However, the cranioplasty could not be performed immediately during the excision of the tumor because of granulomatous inflammation detected in surgery. Based on the type of surgery, the location of the osteoma with extension into the sinus, the high risk of neurological complications, and the microbial environment of the medical facility, the clinical team, in collaboration with the hospital's clinical pharmacologists, decided to implement antimicrobial therapy as part of the patient's treatment plan. Following the surgical removal of the osteoma, the patient was prescribed a course of antimicrobial therapy. The treatment plan included the administration of 1000 mg of Cefepime twice a day and 500 mg of Metronidazole once a day for 7 days after the procedure. Acetazolamide was recommended for the prevention of irregular liquorrhea. The patient was discharged with no symptoms on post-operative day 7. The post-operative 6th-month MRI confirmed no residual tumor. Six months later, the patient was hospitalized to provide a cranioplasty of the defect by a Synicem Cranioplasty (Fig. 2G).

Discussion

Osteomas are benign, slow-growing bone tumors that primarily originate from the paranasal and craniofacial sinuses [1]. These tumors account for a small proportion of primary bone tumors, with only 0.03% of biopsied primary bone tumors being identified as osteomas [2]. Our institution has encountered approximately 1-2 osteoma cases annually, but this case represents the first time we have performed surgical treatment of a sizeable osteoma. The surgery helped to normalize the patient’s proptosis and lateral gaze palsy. The traditional procedure for removing huge osteomas was the open approach, and the presence of orbital extension and the need for bone reconstructing had a big impact on the preoperative choice. The tumor was a massive 7x4x3 cm, with a smaller portion measuring just 2x1x1 cm. In addition, the osteoma expanded from the frontal sinus to the orbital cavity. The complaints about the 5-year-long headache of the patient could be associated with chronic frontal sinusitis. The enormous osteoma, which had an extensive intracranial extension and orbital bone involvement, was indicated for the pterional incision. The protection of the underlying brain and the restoration of cranial form required the reconstruction of bone abnormalities. Autologous bone grafts, titanium mesh, polyethylene sheets, and hydroxyapatite cement may be utilized [7] if an enormous part of the bone has been destroyed. In our case, we used an acrylic cranioplasty to repair the bone defect of the anterior wall of the frontal sinus.

The osteoma is a slow-growing benign tumor with a mean speed of growing 1.66mm/ per year [8]. It is hard to define the etiology of the disease and whether it could be derived from environmental, embryological, and genetic factors. Several case reports mention that the patients had head trauma long before the diagnosis of osteoma [9]. In frontal sinus osteoma reviews, 5-7% of the patients who had osteoma responded that they had head trauma earlier in their life [10]. Our patient also stated that she had head trauma at the age of 2.

Conclusions

The extended tumor with intracranial or intraorbital involvement impacted diffuse headaches proptosis of the

patient's right eye. The open surgery performed on the giant osteoma was a successful example of removing bone tumors and reconstructing the frontal sinus and frontal lobe bone. The masses were removed, and the patient no longer had partial limitation of eye movement, which was the main consequence of the expanded tumor. The lateral rectus palsy regenerated, and the ability to lateral ocular movement was regained. The damaged supraorbital part of the frontal bone was dissected and reconstructed. Surgical approaches to the orbit require a multidisciplinary approach involving neurosurgeons, ophthalmologists, clinical pharmacologists, and otolaryngology-head and neck surgeons.

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Ethic approval and consent to participate: The photographs are completely unidentified and personal details are not mentioned in the text. The authors are accountable for all aspects of the work and for ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Case Report: Vesicular Toxicodermia Induced by the Scabies Mite Sarcoptes Scabiei

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Abstract

This article analyzes a clinical case of vesicular toxicodermia caused by infection with the scabies mite Sarcoptes scabiei. The focus is on a female patient who, according to her medical history, noticed the development of intense itching and rashes on her hands and feet after using an antiseptic. Initial treatment provided no relief, and further investigations confirmed the presence of the scabies mite. The article emphasizes the importance of a comprehensive approach to diagnosing and treating such clinical cases, including careful monitoring for allergic reactions to antiseptics and other potential irritants. Special attention is given to the necessity of etiological therapy directly targeting the scabies pathogen, as well as symptomatic treatment to alleviate itching and inflammatory manifestations.

Keywords: Vesicular toxicodermia, scabies mite Sarcoptes scabiei, scabies complication.

Introduction

Toxic-allergic dermatitis, or toxicodermia, is an acute inflammation of the skin caused by exposure to allergenic or toxic-allergenic factors, which can enter the body parenterally, through food, or in the form of vapors and aerosols [1, 2]. These factors can include a wide range of substances such as drugs, chemicals, and even biological agents. When these substances enter the body, they can trigger an immune response that manifests as skin inflammation. The severity of the reaction can vary, ranging from mild rashes to severe skin damage. Furthermore, the pathogenesis of toxicodermia often involves both immediate and delayed hypersensitivity reactions, contributing to its complex clinical presentation.

The French dermatologist J. Jadassohn first proposed the term «toxicodermia» in 1896. This condition most commonly occurs as a side effect of medications [3]. Although pathological reactions can develop to any drug, including antihistamines and glucocorticosteroids, toxicodermia is most frequently associated with the use of antibacterial agents, antiepileptic drugs, and allopurinol. The development of such rashes is linked to the predominance of CD4 and CD8 T-lymphocytes and delayed-type hypersensitivity [4]. This clinical case presents an example of toxicodermia as a complication of atypical scabies.

Case presentation

Patient T. presented with complaints of itching and rashes on the palms, shins, and feet. Disease history: the complaints began on October 26, when she noticed the appearance of isolated vesicular rashes on the skin of her palms, feet, and shins, which then spread further. She associated this condition with the use of an antiseptic at work. Over the past two weeks, she has noted the appearance of blisters. She was consulted

by an allergist at her place of residence and was prescribed Prednisolone 90-60-60 mg. She noted temporary improvement with the corticosteroid treatment, but the skin manifestations progressed over time. She received Metronidazole, Cefazolin, and Azithromycin for three days. Upon a repeat consultation with the allergist, Azithromycin was replaced with Ceftriaxone (antibiotic therapy was initiated based on signs of inflammation in the complete blood count). Despite the ongoing comprehensive therapy, her condition did not improve. She noted the bursting of vesicles, persistent skin itching, with increased intensity at night, making it difficult to sleep.

Allergic history: In 2014, she had a similar episode of rashes during her first pregnancy at 19-20 weeks, for which she received inpatient treatment with Prednisolone and was discharged with improvement. Occupational history: She works as a doctor, daily sanitizes her hands with antiseptic, and wears latex gloves.

Local Status: On the skin of the palms, feet, and shins, there are vesicles and papules with a diameter of 2-3 mm, oozing, linear scratch marks, and crusts (Figure 1).

Complete Blood Count (23.11.2022): Hemoglobin (HGB) – 138 g/L; Erythrocytes (RBC) – 5.110^12/L; Color Index – 0.81; Hematocrit (HCT) – 40%; Platelets (PLT) – 323.010^9/L; Leukocytes (WBC) – 7.1*10^9/L; Segmental Neutrophils (NEUT) – 73%; Basophils (BASO) – 6%; Lymphocytes (LYMPH) – 21%; Erythrocyte Sedimentation Rate (ESR) – 11

Figure 1 – Clinical Condition of the Patient on the Day of Presentation

Figure 2a – Dynamics of the Patient's Clinical Condition During Treatment – Patient's Condition on Day 5 of Treatment

Figure 2b – Dynamics of the Patient's Clinical Condition During Treatment – Patient's Condition on Day 5 of Treatment

Figure 2c – Dynamics of the Patient's Clinical Condition During Treatment – Patient's Condition on Day 7 of Treatment

mm/h. Biochemical profile (23.11.2022): Total Protein – 80; Alanine Aminotransferase – 16.9; Aspartate Aminotransferase – 20.0; Total Bilirubin – 10.9; Direct Bilirubin – 3.4; Glucose – 6.8; Urea – 5.6; Creatinine – 62. Coagulation Test (23.11.2022): Activated Partial Thromboplastin Time – 34.0 sec; International Normalized Ratio – 1.07; Prothrombin Index – 93%; Prothrombin Time – 15.0 sec; Thrombin Time – 13.4 sec.

On 30.11.2022, the patient visited the Regional Allergology Center "DiVera," where she was diagnosed with mild vesicular toxicodermia. The prescribed treatment included a hypoallergenic diet and the following medications: Prednisolone 90 mg (GCS) with isotonic NaCl solution 100 ml, administered intravenously once a day for 5 days; Cetirizine 10 mg (H1-histamine receptor blocker), 1 tablet once a day for 10 days; topically, Methylene Blue 3 times a day for 7 days. The patient was referred for further tests, including total IgE and specific IgE to latex, and a skin scraping for the detection of the scabies mite (Figure 2).

From the 5th day of therapy, the treatment regimen was changed to Prednisolone 5 mg, 1 tablet once a day in the morning; Cetirizine 10 mg, 1 tablet once a day; and Methyluracil cream applied topically twice a day.

Skin scraping for the detection of the scabies mite was positive. The diagnosis was established as atypical scabies without burrows, complicated by mild vesicular toxicodermia.

The patient was referred to a dermatologist at the dermatovenereology dispensary for further consultation.

Discussion

This article presents an example of toxic-allergic dermatitis against the background of scabies. The clinical case describes the severity of the disease, the dynamics of clinical symptom development, and the complexity of differential diagnosis and treatment.

Human scabies is a contagious skin disease caused by the parasitic mite Sarcoptes scabiei var. hominis. It is a common skin condition that remains a serious public health concern worldwide [5]. The clinical pathological signs of scabies are generally divided into two categories, depending on the type of hypersensitivity reaction: immediate immune response type I, mediated by antibodies [5-7], or delayed cell-mediated immune response type IV [8-10]. Type I reactions are characterized by immunoglobulin (Ig) E-mediated activation of mast cells and eosinophils, whereas type IV reactions involve sensitized T-cells that either cause direct damage or activate other leukocytes [11].

A meta-analysis by Næsborg-Nielsen in 2022 showed that the immediate immune response associated with type I hypersensitivity reaction in the context of scabies is primarily driven by a combination of IgE, mast cells, and eosinophils, followed by the release of histamine and other pro-inflammatory cytokines. The immune response associated with type IV hypersensitivity more frequently involved the proliferation of macrophages, neutrophils, and B-cells [12].

The study by Abd El-Aal in 2016 demonstrated elevated levels of total IgE in scabies [13], and the Australian study by Walton in 2010 found that patients with scabies had higher levels of specific IgE to recombinant scabies antigens compared to the control group [14]. Ito's 2011 study confirmed the presence of mast cells and basophils in the skin of scabies patients [15]. Upon activation, mast cells and basophils rapidly produce TNF-α, IL-6, Th2 cytokines IL-4, IL-5, and IL-13, which are key molecules responsible for Th2-type allergic inflammation [16].

Abd El-Aal's 2016 study also demonstrated the involvement of cytokines IL-10, IL-6, INF-γ и TNF-α in the immune response to scabies [13]. These cytokines play a crucial role in activating macrophages, which were found in small quantities in the skin of scabies patients. It was hypothesized that in the early stages of infestation, mites suppress the ability of macrophages to migrate to the site of inflammation, allowing the mites to grow and establish themselves [17]. Alongside macrophages, neutrophils are an essential part of the innate immune system in the development of type IV hypersensitivity. Luo's 2016 study presented histological data from skin lesions in 44 cases of bullous scabies, showing that neutrophils were the predominant inflammatory cell infiltrates [18]. In another similar study, 25 skin biopsies from scabies patients showed the presence of dermal neutrophils in 52% of cases [19].

At the XI Scientific and Practical Conference of Dermatovenereologists and Cosmetologists, a clinical case from 2016 to 2017 at the 4th department of the GBUZ "GorKVD" was described, where 15 patients with a diagnosis of scabies were treated. From the disease history, it was found that all patients had been treated at district dermatology and venereology clinics with diagnoses of allergic dermatitis and toxicodermia, receiving therapy without effect. Against the background of antiallergic therapy, the skin process progressed. Skin scrapings revealed a large number of scabies mites in all patients. Because an incorrect diagnosis was initially made, the treatment of the patients took longer than necessary. After detoxification, desensitization, and antibacterial therapy, all patients showed improvement, and the clinical symptoms of the disease decreased [20].

Conclusions

A thorough analysis of the medical history is a key element in diagnosing toxicodermia, involving the identification of similar symptoms in the patient's history, occupational risk factors related to the disease development, and the use of medications, among other aspects. In the clinical case under consideration, difficulties arose in identifying causal relationships with the etiological agent due to atypical clinical manifestations. The discussed example highlights that a comprehensive methodology in choosing diagnostic approaches is necessary for successful differential diagnosis and determination of the clinical diagnosis.

After referral to the dermatologist at the dermatovenereology dispensary, the patient was prescribed specific treatment for scabies, including Permethrin cream applied topically to all affected areas of the skin and oral Ivermectin. Additionally, symptomatic treatment with antihistamines and continued topical corticosteroids was recommended. Follow-up after two weeks of this treatment regimen showed significant improvement in the patient's condition: the vesicular and papular rashes had largely resolved, itching was substantially reduced, and there were no new lesions. This case underscores the importance of considering underlying parasitic infections such as scabies in the differential diagnosis of toxicodermia, particularly in patients with atypical presentations.

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N.K. and A.G.; writing – review and editing, M.I.; visualization, S.M.; supervision, M.I.; project administration, M.I. All authors have read and agreed to the published version of the manuscript.

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