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Health Sciences Quarterly (Health Sci. Q.) is an open-access journal that publishes original research papers, case reports, and reviews, clinical studies covering a wide range of subjects in life sciences and medicine as well as clinical and experimental investigations only in English.

Researchers in health sciences will find much of great use and interest in the Health Sci. Q.

HSQ aims to supply scientists of health with resources in order to provide the scientific knowledge through the publication of peer-reviewed, high quality, scientific papers and other material on all topics related to Medicine, Pharmacy and pharmaceutical sciences, Dentistry, Nursing, Bioethics, History of medicine, Health economics, Pharmacoeconomics, Medical education, Public health, and Epidemiology.

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ORIGINAL ARTICLE

First responders' innovative methodology and curriculum definition for advanced virtual reality training

Zeynep Sofuoğlu[1,2] **Débora Pérez Robles**[3] **Eric Didderen**[4]

Federico Rodrigo Carjaval[3] **Turhan Sofuoğlu**[1] **Aysel Başer**[5]

Jóhanna Noraly Veeneklaas[4]

1 Ambulance and Emergency Physicians Association. İzmir / Türkiye
2 Department of Public Health, Faculty of Medicine, İzmir Democracy University. İzmir / Türkiye
3 Department of Geomatic and Surveying, Universitat Politecnica de Valencia. Valencia / Spain
4 Nederlands Instituut Publieke Veiligheid, The Netherlands.
5 Department of Medical Education, Faculty of Medicine, Izmir Democracy University. İzmir / Türkiye

Abstract

Within the ASSISTANCE Project (Adapted Situation Awareness Tools and Tailored Training Scenarios for Increasing the Capabilities and Enhancing the Protection of First Responders) the development of a novel and advanced training programme is currently underway to adapt to the needs and characteristics of first responders. Once the methodology was ready, a complete training curriculum was prepared in order to probe the concept of the European training network based on online Virtual Reality platforms. The curriculum is composed of subjects, which have been developed with a stepwise approach, taking into consideration the pre-requisites needed for each subject and a gradual increase in difficulty and complexity. These subjects can be divided into two different types: theoretical subjects, which will be taught through the Moodle server and practical subjects, which will be taught through the performance of different virtual scenarios with the available Virtual Reality platforms. Each subject definition includes a short summary of the subject, their main, general and specific objectives as well as their preferred evaluation method and the pre-requisites needed. This paper presents the ASSISTANCE training methodology and the curriculum developed including the preliminary scheduling needed to complete all the proposed subjects.

Keywords: First responders, virtual reality training, curriculum development, step wise approach, androgogy

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Corresponding Author:
Zeynep Sofuoğlu
Email: zeynep.sofu@gmail.com

Introduction

The bombing of Oklahoma City in 1995, the attacks on the World Trade Center in 2001, multiple hurricanes that hit Florida in 2004, and hurricanes Katrina and Rita in 2005 are unforgettable events when First Responders (FR) were inadequately equipped to face the emergency. These events have shown us to what extent the natural and man-made disasters can harm human life. They have also highlighted the important role of first responders in protecting citizens for the health and safety of the population [1,2]. The impact of large disasters like these can have disastrous consequences for the European Member States and affect social well-being on a global level. Each type of FR organisation (e.g. medical emergency services, fire and rescue services, law enforcement teams, civil protection professionals, etc.) that mitigate the effects of these kinds of events is exposed to the unexpected dangers and new threats that can severely affect their personal safety. These structures work together to save lives, protect infrastructure resources and the health of the population, which is to restore normality. Among these, paramedics, fire, and rescue services often referred to as emergency first responders, are often the main units within emergency response teams [1-3]. FRs have to perform their work in chaotic and stressful emergency response situations, making the best decisions quickly, based on information about the disaster at hand and its immediate surroundings [1,2].

The aim of the study was to prepare a curriculum for FRs to gain better knowledge and develop skills according to their training needs, which is the first step of the training programme development.

According to Hermans et al., in general adults are a heterogeneous group with a large variety of learning preferences, learning ambitions, prior knowledge and personal circumstances [4,5]. Cercone adds that most adult learners are highly motivated and task-oriented, with Lee et al. expanding on this stating that adults are more independent and self-regulated in their learning [5,6].

Tretsiakova-McNally et al., pose that experience, including making mistakes, provides the basis for learning activities. They also state that adult learning is problem-centred rather than content-oriented, and that adults are most interested in learning subjects that have immediate relevance to their job or personal life [3]. Adults have certain limitations, such as multiple responsibilities (e.g. families and jobs), physiological limitations, and difficulty in dealing with technology (Lee, K., et al., 2019). To overcome this they need real hands-on experience. Virtual Reality (VR) technology offers a broad opportunity to meet the various expectations of adult education theory and enhances the skills and capabilities of FRs [3,4]. Cercone also states that primarily due to their busy schedules and the convenience of the online format, many adults want to take advantage of online learning environments [5]. The objectives of the study are to understand training needs of the FRs for the use of drones, wearable, and robots to enhance their situational awareness, skills and capabilities and develop a VR training program.

Materials and Methods

Approval for conducting the study was obtained from the Noninterventional Studies Ethics Committee of Tepecik Research and Training Hospital (2019/12-16).

Population; the sample of the study consisted of FRs over the age of 18 living in Poland, Sweden, Spain, Netherlands, and Türkiye. The inclusion criteria were determined as being over 18 years old, working as ambulance, fire fighter, and police FRs in the countries mentioned above. Individuals who did not agree to participate in the study or did not completely fill out the survey form were excluded. Before they started to fill out the survey, all participants consented to participate in the study and provided permission for their data to be used.

Data collection; the data were collected between July, 1-31, 2019 on the Survey Monkey platform. The FR Consortium members from Poland, Sweden, Spain, Netherlands, and Türkiye distributed the questionnaire to the FR agencies in their country. Messages including the invitation to participate in the study and information about the study were included in the email.

Participation in the study was voluntary, and before starting to collect data, the participants were provided with an informed consent form to confirm. No monetary or non-monetary incentives were offered to the participants for their participation.

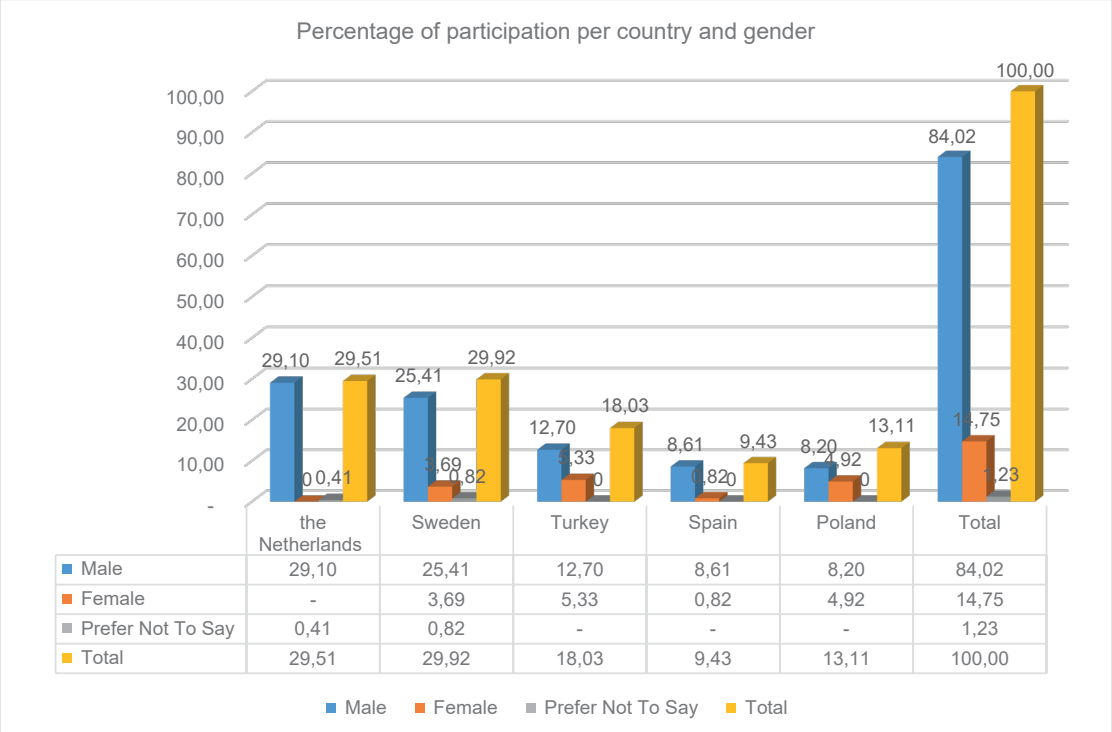
Survey form; the open-access online survey form consisted of questions on the sociodemographic and their current mission type (5 items), their experience with drones, wearable, and robots as situational awareness tools, their preferred learning method(s) (27 items). Totally 32 questions.

Results

In total, 244 responses were received to the developed questionnaire. The country with the highest participation was Netherlands with 29.51% and all respondents were male, excluding one person who did not specify their gender. The participation rate of other countries were 29.92% Sweden, 18.03% Türkiye, 9.43% Spain, and 13.11% Poland (Figure 1).

The majority of the respondents (31%) were males between 35 and 44 years old; furthermore, most women who participated in the survey were between 25 and 34 years old (7% of all respondents). The percentage of FRs between 45-54 years old was 23% and 7% were between 55-64 years old. Most of the respondents perform fieldwork as their mission type (31.14% out of 244 respondents), whereas 18.44% (n:76) of respondents also work in a command/ dispatch function, 18.44% (n:45) in training, 15.16% (n:37) in a managerial function (office), and 16.52% (n:33) in technical support. Most men (42%) work in the field, while 25% of the women work in the field. Three participants worked in emergency services for less than one year and one participant worked for 45 years. The median was 16.5 years, the arithmetic mean was 13.29 years and the mode was 20 years for working years in emergency services as FRs.

The majority of FRs have little experience using the feedback from the proposed technologies. 44.5% of the participants (n:144) do not have any professional experience. They answered 'None' when asked "How many times did you professionally use feedback of drones/wearables/ robots?". Only 0.8% of all respondents (n:2) have used all technologies more than 10 times. The country with the most-trained number of respondents in terms of the use of drones was Poland (78%). The least trained FRs among the



	the Netherlands	Sweden	Turkey	Spain	Poland	Total
Male	29,10	25,41	12,70	8,61	8,20	84,02
Female	-	3,69	5,33	0,82	4,92	14,75
Prefer Not To Say	0,41	0,82	-	-	-	1,23
Total	29,51	29,92	18,03	9,43	13,11	100,00

Figure 1. Percentage of participation per country and gender.

respondents were from Spain (16%) and Sweden (32%). In their free time, 97 FRs (39.7%) do not use the proposed technologies.

FRs have the most experience in gaining knowledge regarding using technical tools (drones, wearables, robots) by handbooks (n:38; 57.6%), and workshops (n:37; 56.1%). For working with drones specifically lectures/ seminars, workshops and handbooks are the most used for gaining knowledge (all n:20; 55.6%). 55% (n:21) of the FRs were satisfied (it was 'fine, good or very good') with the training they have received.

The preferred ways of gaining knowledge and skills were "Training with digital solutions (AR/VR)" with 147 respondents (60.25%) and "E-learning" with 144 respondents (59.02%). The predominant choice for gaining knowledge and skills for other training options were "Workshops" with 120 (49.18%) respondents, "Lectures /

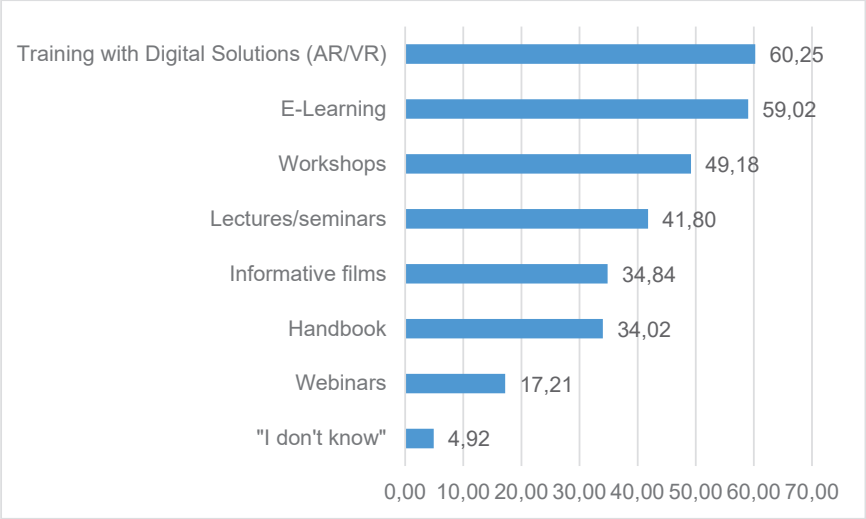


Figure 2. Distribution of preferred ways of gaining knowledge and skills.

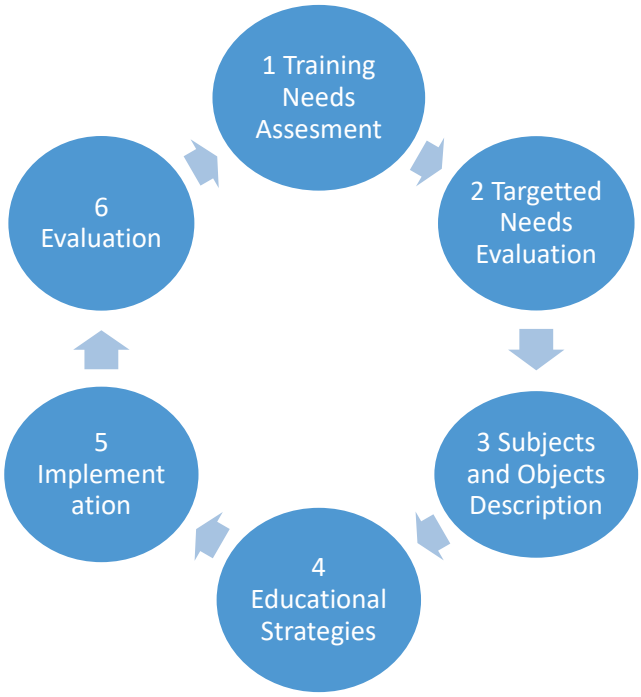


Figure 3. Training curriculum development phases (adapted from Kern's six-step approach to curriculum development [6].

Seminars" with 102 (41.8%), "Informative films" with 84 (34.84%), "Handbook" with 83 (34.02%), and" Webinars" with 42 (17.21%) respondents (Figure 2). The training curriculum was centred on learning with virtual, augmented and mixed reality and elearning for training different FR organisations was highly rated. The target group for the training are European FRs; mainly, but not limited to, paramedics, police officers and firefighters. Based on the training methodology, a tailored step-by-step training curriculum has been composed, consisting of training objectives per step as well as the methods for their evaluation. Development and planning steps of the Training Curriculum (Figure 3):

1. Training Needs Assessment
2. Targeted Needs Evaluation
3. Subjects / Objects Description
4. Educational Strategies
5. Implementation
6. Evaluation [6]

As stated previously a solid literature review, questionnaires and group discussions helped to establish the training needs and methods described in the training methodology as the first step in developing the curriculum. The Targeted Needs Evaluation step, which points the methodology evaluation criteria, has also been defined in the methodology.

The curriculum description includes several subjects that will cover all the necessary learning aspects for the different first responders' organisations (ambulance staff, firefighters, and police) which will test the Advanced VR Training Platforms. Additionally, the curriculum also covers the educational strategies, implementation (scheduling), and evaluation of the subjects.

As such the whole training curriculum developed covers eight subjects, organised taking into consideration the pre-requisites needed for each subject and a gradual increase in the difficulty and complexity. Each theoretical subject (1 to 4) is composed of several lessons. These lessons include the general and specific objectives of each subject.

Additionally, each subject has a determined total duration according to the time needed to read all the material, the exercises, and to conduct the evaluation. This is necessary to build the overall training schedule during the project. Finally, each subject has a mentor, or subject specialist, who is the designated point of contact for concepts which could be problematic for the main trainer. The defined curriculum is composed of the 8 subjects that can be seen in Table 1.

Table 1. Training subjects.

Subject Name	Description
1. Background Knowledge	The first part includes all the minimal background knowledge required to understand the Virtual reality, Augmented Reality and Mixed Reality concepts to help trainees to continue onto the next part of the training.
2. Virtual Reality Platforms	The second part comprises all the subjects that describe the Virtual Reality Platforms and their usage.
3. Virtual Reality Platforms Usage	
4. Virtual Reality Scenarios	The third part is composed of the Virtual Reality Scenarios description.
5. Simple Virtual Reality Scenario	The fourth part provides the performance of Scenarios described in subject 4 through different training sessions. The virtual scenarios described in this subject shall be performed by the trainees through the different VR platforms available in the Consortium within subjects 5 to 8.
6. First Pilot Virtual Reality Scenario	
7. Second Pilot Virtual Reality Scenario	
8. Third Pilot Virtual Reality Scenario	

A brief subject description of the planned lectures is given below:

Subject 1: Background Knowledge

This subject includes the minimum background knowledge that is required to understand Virtual Reality, and Mixed Reality concepts. For example, definitions, examples, online VR platforms for the general public and specific training applications that are currently available to be used by the FRs. The different lessons that comprise Subject 1 according to the Moodle subject structure along with its prerequisites and evaluation method used are described in Table 2.

The rest of the subjects have a similar structure to the one described in Table 2 and they can be consulted in the Moodle server. For subjects 2 to 4 only descriptions of the subjects have been included in this section in order not to make it too extensive. The whole content described in the article is available in the different lessons of Subject 1 at the Training Moodle server.

As an example of the information stated in Table 2, the subjects' table of contents, a screenshot of the content of Subject 1 is included in Figure 4.

Subject 2: Virtual Reality Platforms

Once the background knowledge on VR has been introduced in Subject 1, in Subject 2 the VR platforms available to the Consortium are described. This way the trainees will have an overall description of each VR platform they are going to use during the training exercises before they study the manuals and/or explanatory videos in subject 3, which will enable them to start using these VR platforms. This progressive introduction in the VR applications and available platforms forms a part of the stepwise approach followed in the whole training curriculum development.

Table 2. Subjects Structure.

Lesson Number	Subject Content	Prerequisites	Evaluation method
1.L0	Lesson Introduction	None for subject 1	Review Quiz for subject 1
1.L1	Virtual reality concept	None for subject 1	Review Quiz for subject 1
1.L2	Virtual reality open platforms (Gaming)	None for subject 1	Review Quiz for subject 1
1.L3	Training through Virtual reality platforms	None for subject 1	Review Quiz for subject 1
1.L4	FR training using Virtual reality platforms	None for subject 1	Review Quiz for subject 1

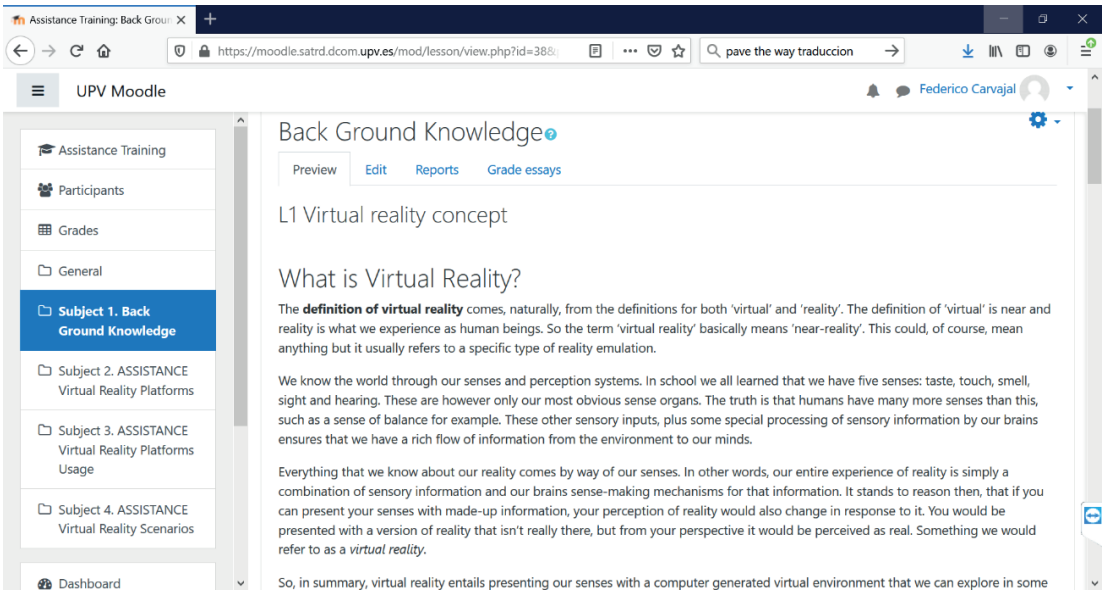


Figure 4. Screenshot showing Subject 1: content for VR general concepts description in the Training Moodle server.

In the first lesson of this subject, the trainees will find a general description of the VR Training Platform (SIMTAC) of Universitat Politécnica de Valencia (UPV) shown in Figs. 5,6 [7] the Instituut Fysieke Veiligheid (IFV) VR Advanced Disaster Management Simulation (ADMS) [8] system shown in Figure 7-8 and VR system of Centrum Naukowo-Badawcze Ochrony Przeciwpożarowej (CNBOP) [9] shown in Figure 9-10; in order to get to know the VR platforms main characteristics before they start learning how to use the platforms in Subject 3.

Subject 3: Virtual Reality Platforms Usage

As the background knowledge on VR functionality and VR platforms has been introduced in Subject 1 and 2, in Subject 3 the dedicated VR platforms (UPV VR, IFV VR, CNBOP VR) usage is described. In this subject, instruction manual on how to operate with each platform provided in the project are shown. Moreover, photos and videos, showing how to use and operate different functionalities necessary to complete the training scenario, are included.

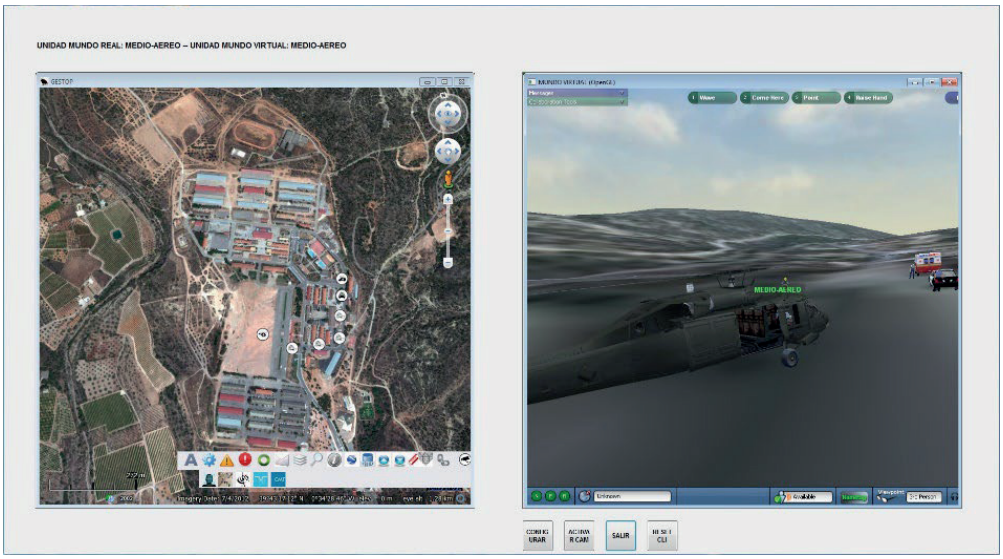


Figure 5. SIMTAC platform showing real Command and Control System and virtual world.

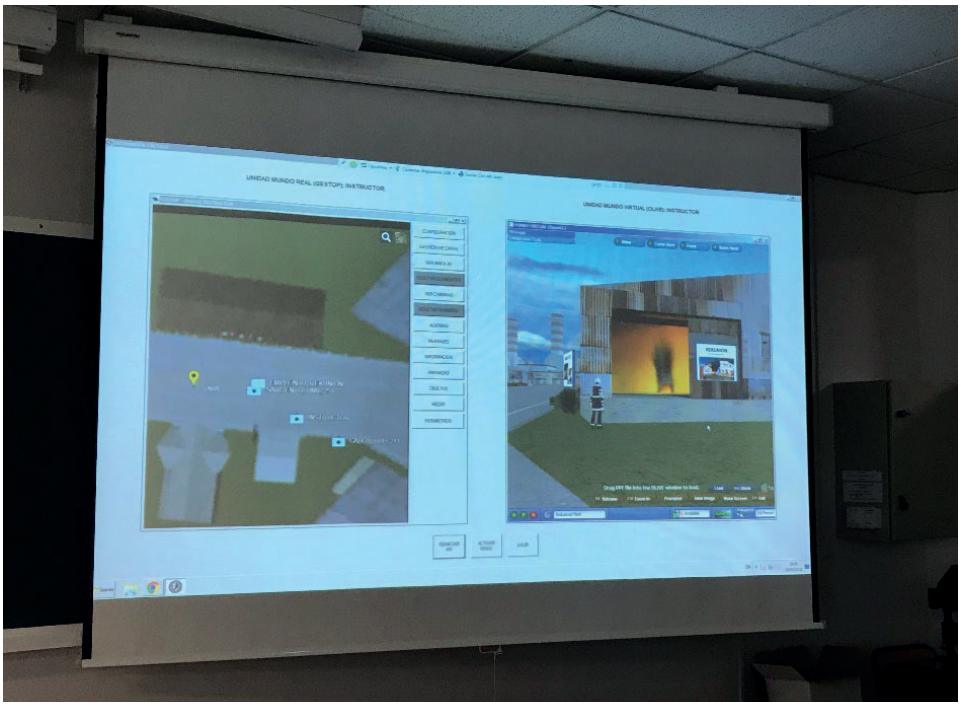


Figure 6. SIMTAC platform used during a course for the Valencia Firemen Department.

Subject 4: Virtual Reality Scenarios Descriptions

This subject describes the types of scenarios that will be carried out using the three VR platforms available in the Consortium for Subjects 5-8 in the curriculum. Subject 4 clarifies the link between the theoretical knowledge and its application in the daily work of the students.

The scenarios encompassed by Subject 5 are intended to be an introduction to the three VR platforms used in the ASSISTANCE project. The scenarios comprising Subjects 6-8 will be used for training in conjunction with the three demonstrator pilots that will be conducted in Türkiye (Subject 6), Netherlands (Subject 7), and Spain (Subject 8).

Subject 5: Simple Virtual Reality Scenarios

This subject is the first practical one and therefore will be taught through the use of the different VR platforms available in the Consortium. This will be carried out in various scheduled sessions whereby the FRs will access the VR platforms to get to know their features and accomplish different scenarios. In this subject, the simplest VR scenarios described in Subject 4 will be executed via remote sessions that will be agreed and scheduled between the FRs participants and the VR platforms providers.

Figure 7. ADMS scenario example.

Figure 8. ADMS training - commander giving commands using a 180-degree screen with ADMS.

For these subjects the VR scenarios described in Subject 4 for the different project pilots will be carried out via remote sessions that will take place during the project demonstrations in Türkiye, the Netherlands and Spain.

Evaluation Criteria

As stated earlier, the training curriculum is composed of several subjects, which have different types of content. The first four subjects are more theoretical and will be taught through an online learning platform (Moodle server) hosted by UPV. The last four subjects of the curriculum (5 to 8) will be more practical and will be taught through VR reality scenarios using the three VR platforms available in the Consortium. Due to these content differences (theoretical and practical), there will also be differences in the evaluation criteria assigned to each type of subject. The criteria will be based on documented legal requirements, standards and practices as well as opinions collected.

Evaluation criteria for the first four theoretical subjects

For the first four subjects, taught through the Moodle server, the Moodle evaluation features are used for evaluation. A Quiz Review for each subject is the main tool for evaluating the level of knowledge acquisition of the trainees. This

Figure 9. CNBOP Monastery Fire scene.

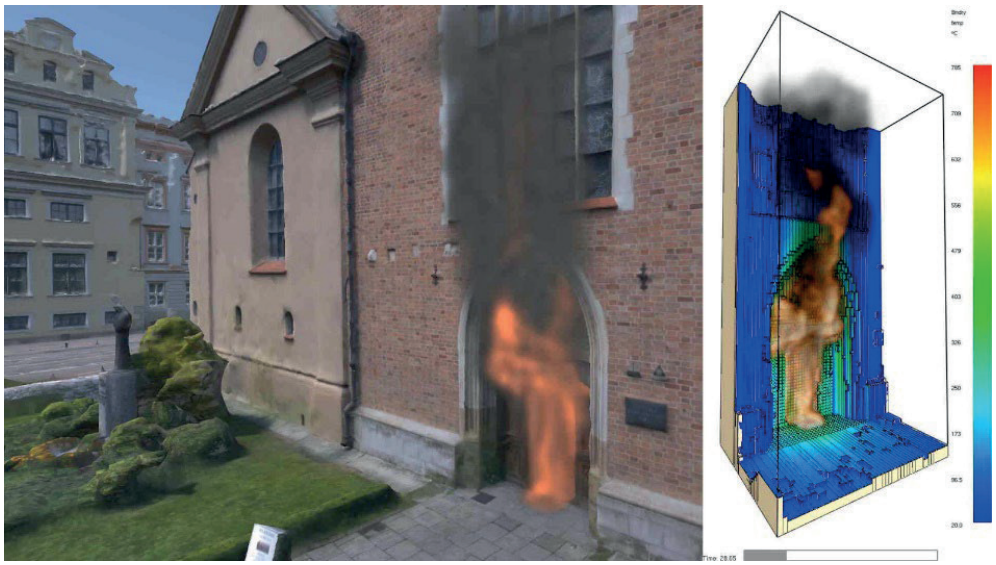


Figure 10. CNBOP Fire visualisation in the application.

Quiz Review is composed of 10 questions taken automatically and randomly by the system from a predefined question bank. The questions are based on the objectives (main, general, specific) of each subject. The quiz answers determine whether the learners understand what they are expected to learn, how the learning process is conducted, why it is important and how the learning outcomes can be applied to their daily work.

The evaluation criterion applied to all subject quizzes is that the minimum grade to pass each quiz must be a score equal to or higher than 8 correct answers. This grade configuration in the Moodle platform is described in Figure 11. The evaluation criterion also states that the trainee

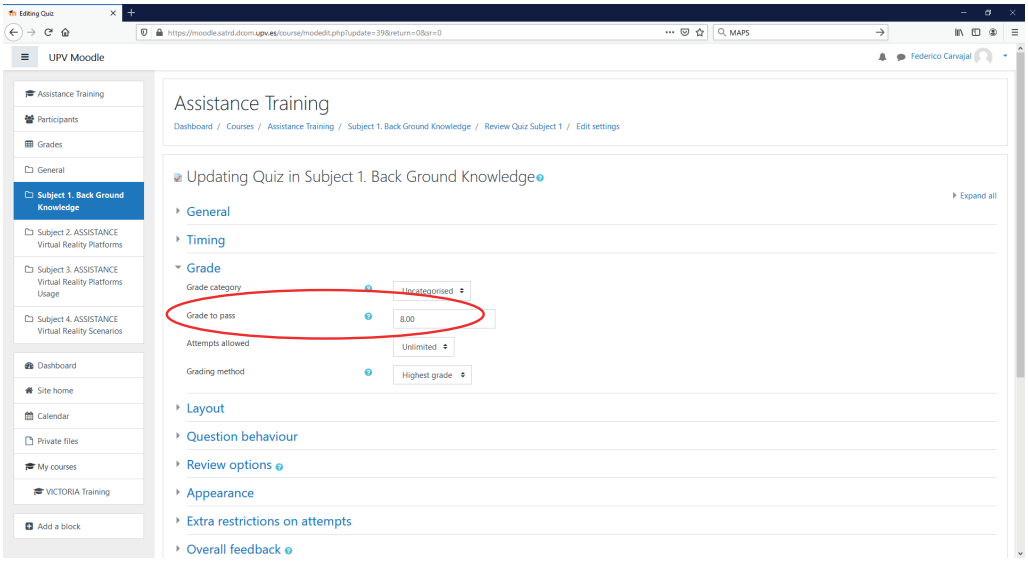


Figure 11. Grade to pass configuration.

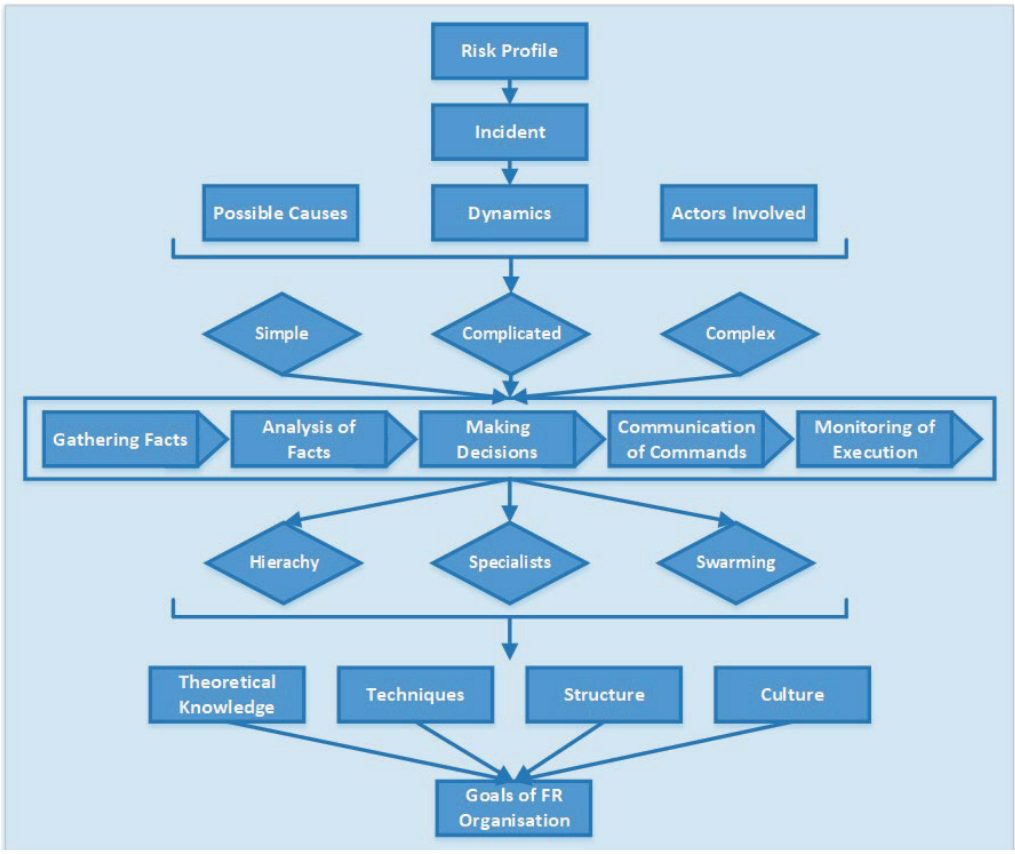


Figure 12. FADCM model used for evaluation of trainees of IFV VR platform.

will not be able to access the next subject unless a passing grade is obtained for the current Quiz Review. This restriction has been also configured in the Moodle platform in order to ensure the knowledge acquisition of all subjects.

Evaluation criteria for the practical subjects

Regarding the practical subjects (5, 6, 7, and 8) evaluation criteria will be based on the achievement of the objectives/goals of each scenario. As the practical subjects will be composed of different scenarios that will be performed using different VR platforms, these evaluation criteria will depend on the virtual platform used.

The evaluation criteria will assess the learner's capabilities for facing complex situations and will generally be based on the FADCM model. By combining the steps of the models in the literature for the training of the front-line crews, a model in which the decision is formulated in an order has been obtained by Groenendaal in 2015. FADCM is a model that places situational awareness especially in firefighting. FADCM stand for Facts (gathering of information), Analysis (analysing the problem), Decision, Communication (issues to order) and Monitoring (Figure 12) and it is a tool to generate qualitative evaluation criteria. The model shows step-by-step the abilities and limitations of first responders and how they can apply their knowledge in practice [10,11].

Discussion

The aim of the project is twofold: On the one hand the project will protect and help the different types of FR organisations that work together during the mitigation of large disasters (natural or man-made) and on the other hand ASSISTANCE will improve the FRs capabilities and skills for facing these kinds of events. For accomplishing the second main objective the training methodology has been defined and a stepwise tailored training curriculum has been composed, describing what to do, when and where to do it in terms of training activities and to what type of FRs each part of the curriculum addressed. The second part of the proposed training aims to improve the ability of FRs to confront complex situations, to provide them with advanced training based on VR and MR, customised to their organisational characteristics.

The ability of first responders to understand the situation and to accurately predict the flow of events in major disasters is defined in the literature as situational awareness. It is as crucial as finding the right balance between time, speed, and rigor when making decisions during emergencies. Establishing this balance is possible by simulating the situation before the actual disasters occur. While developing the curriculum, it is very important for pedagogical designs to use new technological constructivist approaches to simulate emergencies with a high probability of occurring [12-14].

In the literature, we see that most adult learners are highly motivated, problem-centred and task-oriented, that is they are more interested in learning about matters most relevant to their work. According to the literature adults are independent and self-regulated in their learning [3-5]. The use of VR techniques, Moodle platform and simulation scenarios in the project shows the constructivist approach of the newly developed curriculum that has been supported by the literature on the adult learning principles and technology-based curriculum perspectives.

Nowadays different FR organisations cooperate together to face large and complex disasters that in some cases can be amplified due to new threats such as climate change in the case of natural disasters (e.g., floods and wildfires, etc.) or the increase of radicalisation in the case of man-made disasters (e.g., arsonists that burn European forests, terrorist attacks coordinated across multiple European cities). The impact of large scale disasters such as these can have disastrous consequences for the European Member States and affect social well-being on a global level. Each type of FR organisation (e.g., medical emergency services, fire and rescue services, law enforcement teams, civil protection professionals, etc.) that mitigates the effects of these kinds of events is exposed to unexpected dangers and new threats that can severely compromise their personal safety. Therefore, the FRs' skills and capabilities have to be enhanced through tailored training based on new learning approaches adapted to each type of FR organisations' needs and using the advanced

VR training platforms via the European training network for FRs.

This paper highlights the main steps in the development of a novel methodology and training approach. This training programme includes a combination of lectures, virtual reality and scenarios exercises.

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Conflict of interest

There is no conflict of interest between the authors of this study.

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ORIGINAL ARTICLE

Investigation of the protective effect of vitamin K1 on the heart in streptozotocin induced type 1 diabetes model

Abdülkadir Bilir[1] **Esra Aslan**[2]

1 Department of Anatomy, Faculty of Medicine, Afyonkarahisar Health Sciences University. Afyonkarahisar / Türkiye
2 Department of Histology and Embryology, Faculty of Medicine, Afyonkarahisar Health Sciences University. Afyonkarahisar / Türkiye

Abstract

Maternal and fetal diabetes are directly associated with increased morbidity and mortality risk. Along with this increased risk, the incidence of congenital malformations in newborns also increases depending on the mother's diabetes. Vitamin K1 is used as a therapeutic and protective agent in diabetes and various clinical conditions. For this reason, it was aimed to investigate the effect of vitamin K1 on chick embryo hearts immunohistochemically and morphologically by creating type 1 diabetes mellitus with streptozotocin in a chick embryo model. In our study, 5 different experimental groups will be created and a total of 50 SPF fertilized eggs, 10 in each group, will be used. The first group will be the control group, the second group will be the diabetes group, and the other three groups will be the treatment groups given different doses of vitamin K1. All solutions will be given on the 12th day of incubation, and the hearts of all embryos will be analyzed immunohistochemically and morphologically on the 18th day of incubation. It was determined that the weight, length and ventricular thickness of the chick embryo hearts were statistically significantly decreased in the streptozotocin group compared to the control group embryo hearts. It was determined that the heart weights, lengths, and ventricular thicknesses increased depending on the dose of vitamin K1 compared to the streptozotocin group in the groups therapeutically administered vitamin K1 (p<0.05). In addition, caspase-3 expression was also evaluated in our study, and a statistically significant increase was found in the streptozotocin group compared to the control group. Again, as a result of vitamin K1 administration, caspase-3 expressions decreased depending on the applied dose (p<0.05). In conclusion, it was concluded that the therapeutically applied vitamin K1 to diabetes mellitus reduces the degenerative and hyperplastic effects of diabetes mellitus.

Keywords: Chick embryo, diabetes mellitus, heart, streptozotocin, vitamin K1.

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Corresponding Author:
Abdülkadir Bilir
Email: fztabdulkadirbilir@gmail.com

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by abnormalities in lipid, protein and carbohydrate metabolism causing from complete or relative insufficiency of insulin action and/or insulin secretion. The riskiest population for this disease is pregnant women. Because maternal and fetal diabetes are directly associated with increased morbidity and mortality risk [1]. These risks increase in the early and late stages of pregnancy and even may cause congenital malformations in newborns due to maternal diabetes [2–4]. Although central nervous system anomalies and cardiovascular defects are common among these malformations, they are associated with complications that occur especially in the early stages of organogenesis (the first 8 weeks of pregnancy) [5,6].

Cardiovascular defects due to DM include patent ventricular septal defects, ductus arteriosus, and endocardial cushion defects [7]. Despite all clinical interventions to ensure optimal glycemic control during and before pregnancy, the rate of cardiovascular defects in children of diabetic mothers is still higher than in non-diabetic mothers. The mechanisms underlying these defects are not also fully discovered [8]. However, in disorders caused by DM, factors such as changes in metabolic and signaling pathways, beta cell tropism, immunosuppressors, viral infectious agents or hypercaloric diets, and chemical, toxic agents or drugs come to the fore. Alloxan and streptozotocin (STZ), which are toxic glucose analogues specific to beta cells, are toxins that are frequently used to induce experimental diabetes by chemical method and have been used for a long time to create experimental DM in animals [9,10].

STZ is a potent alkylating agent that causes glucokinase function, multiple DNA strand breaks, and glucose transport. It is one of the most commonly used agents in non-surgical DM models. Even a single high dose can cause DM as a result of its toxic [8,11,12]. Vitamin K1 is a form of vitamin K that has proven its therapeutic and protective efficacy in different populations and various clinical conditions worldwide. In the literature, its effectiveness on DM and hyperglycemia has been emphasized [13,14]. For this reason, it was aimed to examine the therapeutic effect of vitamin K1 in chick embryo hearts by immunohistochemical and morphological methods by creating type 1 DM with STZ in the chick embryo model.

Materials and Methods

Ethical Consent

This study was approved by Afyon Kocatepe University Animal Experiments Ethics Committee (49533702/267).

Experimental Animals and Laboratory Conditions

In this study, 50 fertilized 0-day-old specific pathogen-free (SPF) eggs weighing 65±5 g obtained from the Veterinary Control and Research Institute (Bornova, İzmir, Türkiye) were used. The SPF eggs used in the study were incubated in the anatomy laboratory at 70% humidity and 37.5°C. During the incubation period, all eggs were automatically rotated at an angle of 45° to the vertical axis every 2 hours.

Chemicals and Doses

STZ (N-(Methyl Nitroso Carbamoil)-a-D-glucosamine, CAS Number:18883-66-4, Sigma-Aldrich Chemie GmbH, Germany) was dissolved in saline and a stock STZ solution was prepared. The dose of 0.30 mg/egg STZ was determined according to the literature to induce diabetes in chick embryos [10,15,16]. Three different doses vitamin K1 (Konakion 10 mg/ml, Roche) were administered for treatment [13].

Experimental Groups and Experimental Protocol

50 SPF eggs were placed in the incubator with their acute ends down. On the 12th day of incubation, all eggs were randomly distributed into 5 groups, with 10 eggs in each group. The first group was designated as the positive control group and was administered only saline. Other eggs were applied STZ. The first of the groups to which STZ was applied was determined as the negative control group (n=10). Three different doses of vitamin K1 (0.005 mg/egg for low dose, 0.025 mg/egg for medium dose, 0.050 mg/egg for high dose) were administered to the other groups in which STZ was aplied, 3 hours after

the injection. All solutions were administered to the air sack in 0.1 ml volumes with an insulin injector, and the window opened after each application was closed with sterile drape and put back into the incubator. On the 18th day of incubation, all of chick embryos were evacuated from the egg and quickly decapitated. After decapitation, the hearts of all embryos were dissected and routine protocols were performed for morphological and immunohistochemical examination.

Morphological Measurements

Firstly, the dissected hearts were weighed with precision balance. Photographs were then taken with a stereomicroscope (Carl Zeiss Stemi 2000-C). For better histopathological and immunohistochemical examination, hearts were rinsed in cold saline, and fixed in 10% formaldehyde solution and transversely cut. Cuts were made from the ventricular apex to approximately 60% of the length of the heart. Ventricular tissues were routinely processed and embedded in paraffin and 5 micromillimeter sections were taken. The septomarginal trabecula was used to maintain a relatively stable position to allow measurements of the ventricular wall at the same location in each heart. Hearts were stained with Hematoxylin and Eosin (H&E) solution for routine histology [17,18]. Image Analysis Software program (NIS Elements Nikon, Japan) used to measure the thickness of the ventricular wall. The right ventricular wall was chosen as the histological target and the thickness of the ventricular walls was measured from 5 different locations (Figure 1).

Immunohistochemical staining

Tissue samples were deparaffinized and dehydrated by taking 5 μm sections on polylyzed slides. It was stained immunohistochemically with caspase-3 primary antibody. Antigen retrieval was performed with heat for 20 min in a microwave oven in citrate buffer (pH 6.0). Endogenous peroxidase activity was inhibited by the application of 3% hydrogen peroxide (H_2O_2). The primary antibody caspase-3 (Anti Caspase-3, NB100-56708, Novus Biologicals, 1/200) was then dropped and incubated overnight. After incubation, horseradish peroxidase (HRP) secondary antibody kit was used as secondary antibody. Sections were incubated with biotinylated secondary antibody for 30 minutes and then incubated with HRP-conjugated streptavidin for 30 minutes. Aminoethyl carbazole (AEC) kit was used as chromogen. Finally, all sections were counterstained with Mayers hematoxylin and sealed with water-based sealing solution.

The histological scoring method used by Wang et al was used to evaluate caspase-3 expression. Scoring of expression was based on the intensity and extent of staining. The mean rate of stained cells was determined semi quantitatively (Figure 2) and scored as follows [19]:

0 for staining <1%, 1 for 1 to 25%, 2 for 26 to 50%, 3 for 51 to 75%, and 4 for >75% of the examined cells. Staining intensity was graded as follows: 0, negative staining; 1, weak staining; 2, moderate staining; 3, strong staining. The histological score (H score) for each specimen was computed by the formula: H score = intensity score × proportion score. All the sections were evaluated under light microscope (Eclipse E-600 Nikon, Japan) and Image analysis was made with Image Analysis Software for assessing the samples.

Statistical analysis

Statistical analysis of the study data was performed with the IBM Statistical Package for Social Sciences (SPSS) Statistics 25.0 program. The normal distribution of data was analyzed with the Shapiro Wilk test. After it was determined that the data were not normally distributed, the Kruskal-Wallis *H* test was used to determine the differences between multiple independent continuous variables, and the Mann-Whitney U test was used to compare the paired groups with Bonferroni correction. P <0.05 were considered statistically significant. Data were presented as median (minimum-maximum)

Results

In our study, 10 SPF eggs were randomly determined for each experimental group. However, due to developmental defects (developmental retardation, lack of vascularization, unfertilization) determined in the embryos during the incubation period or

their death during the incubation period, an average of two embryos from each group were lost. Depending on this loss, the analyzes were evaluated on 8 embryo hearts.

As a result of the study, it was determined that the weight, length and ventricular thickness of the chick embryo hearts were statistically significantly decreased in the STZ group compared to the control group embryo hearts. It was determined that the heart weights, lengths, and ventricular thicknesses increased depending on the dose of vitamin K1 compared to the STZ group in the groups therapeutically administered vitamin K1 (p<0.05). In addition, caspase-3 expression was also evaluated in our study, and a statistically significant increase was found in the STZ group compared to the control group. Again, as a result of vitamin K1 administration, caspase-3 expressions decreased depending on the applied dose (p<0.05). Statistical differences among study result data and groups are shown in Table 1.

Discussion

Diabetes mellitus is one of the common metabolic pregnancy complications related with an increased risk of neonatal and maternal morbidity. Undoubtedly, the cardiovascular system, which is one of the first systems to develop in the fetus, is vulnerable to exposure to hyperglycemia caused by gestational diabetes. Dysplasia of the cardiovascular system, which occurs during the cardiogenesis and organogenesis period as a result of uncontrolled diabetes, often results in neonatal and maternal morbidity. But the biggest concern with diabetes is cardiovascular morbidity rather than mortality [20,21]. Because diabetes-induced morbidity leads to cardiovascular defects and thus disrupts quality of life to a great extent [7,22]. In order to prevent that, the prevention of diabetes during pregnancy has become a basic principle by clinicians. For this reason, antioxidants are used as potential protectors during pregnancy [20,21].

Chick and human pancreatic islets are flimsy against streptozotocin. Therefore, chick embryos are used in experimental diabetic methods instead of mammals. It is also preferred due to its ease of manipulation and sensitivity in antioxidant mechanisms [23].

The primary circulating form of vitamin K is vitamin K1. The efficacy of circulating vitamin K has been successfully demonstrated worldwide in various clinical-based and population-based studies. In previous studies, it has been shown that dietary vitamin K1 reduces risk of type 2 DM and hyperglycemia [13,14]. Therefore, in this study, we aimed to immunohistochemically and morphologically examine vitamin K1 in STZ-induced chick embryo type 1 DM model.

In the literature, Memon and Pratten showed the effect of hyperglycemia on the heart in the chick embryo experimental model created with 20 mM glucose. As a result of the study, abnormal heart development (especially enlargement of ventricular chambers) was detected in embryos treated with glucose [20]. Likewise, Datar et al. examined the exposure of chick embryos to 30, 50 and 100 mM glucose for 24 hours and found that mortality increased with increasing glucose concentrations, especially in the early embryonic stages. However, at stage 21 of Hamburger-Hamilton 100 mM glucose caused 1-2% abnormal heart development [24]. Mohammed et al. investigated the potential cardiotoxic effect of hyperglycemia with hyperketonemia using two in vitro models. As a result of the study,

Table 1. Study result data and statistical differences.

Groups	Weight (g)	Lenght (mm)	Thickness (µm)	Caspase 3
STZ	0.26 (0.2-0.29) [a]	1.02 (0.92-1.3) [a]	647.92 (488.31-805.55) [a]	2 (1-3) [a]
Low Dose	0.13 (0.12-0.13) [a,b]	0.91 (0.84-0.97) [a]	485.01 (364.77-647.776)	5.67 (4-8) [a]
Medium Dose	0.16 (0.12-0.25) [a,b]	0.93 (0.74-0.99) [b]	578.55 (522.37-681.428) [b]	3 (3-6) [b]
High Dose	0.17 (0.15-0.2) [a,b]	1 (0.89-1.13) [b]	624.11 (499.01-724.806) [b]	2 (2-6) [b]
Control	0.19 (0.15-0.22) [b]	1.03 (0.89-1.24) [b]	615.65 (529.98-733.21) [b]	2 (1-4) [b]
***p* value**	<0.001	0.035	0.004	<0.001

a : There is a statistically significant difference with the control group.

b : There is a statistically significant difference with STZ Group.

Data shown as **median (minumum-maximum)**, **g:** gram, **mm:** millimeter, **µm:** mikrometer.

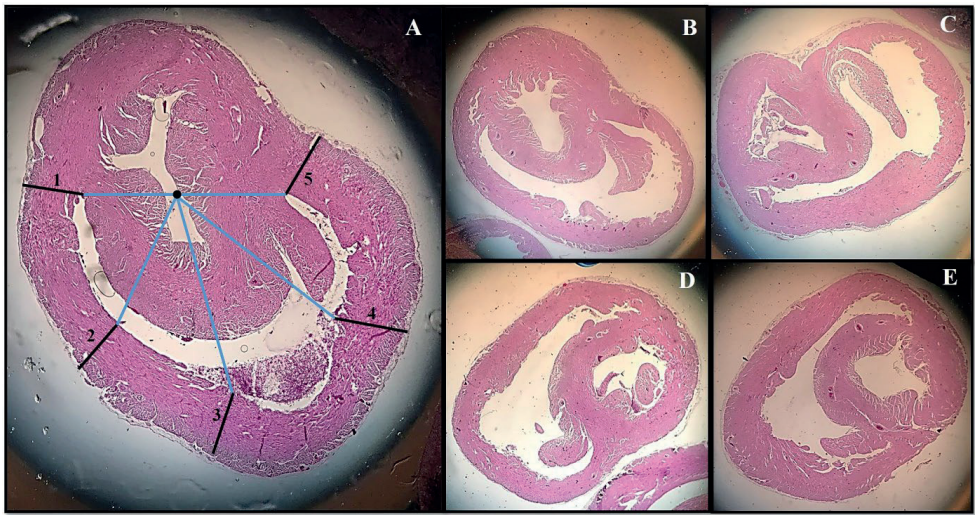

Figure 1. H&E histological sections showing the ventricular wall thicknesses of the experimental groups and morphometric measurements (indicated by radiating lines).
A: Control group, **B:** STZ, **C:** Low dose, **D:** Medium dose, **E:** High dose.

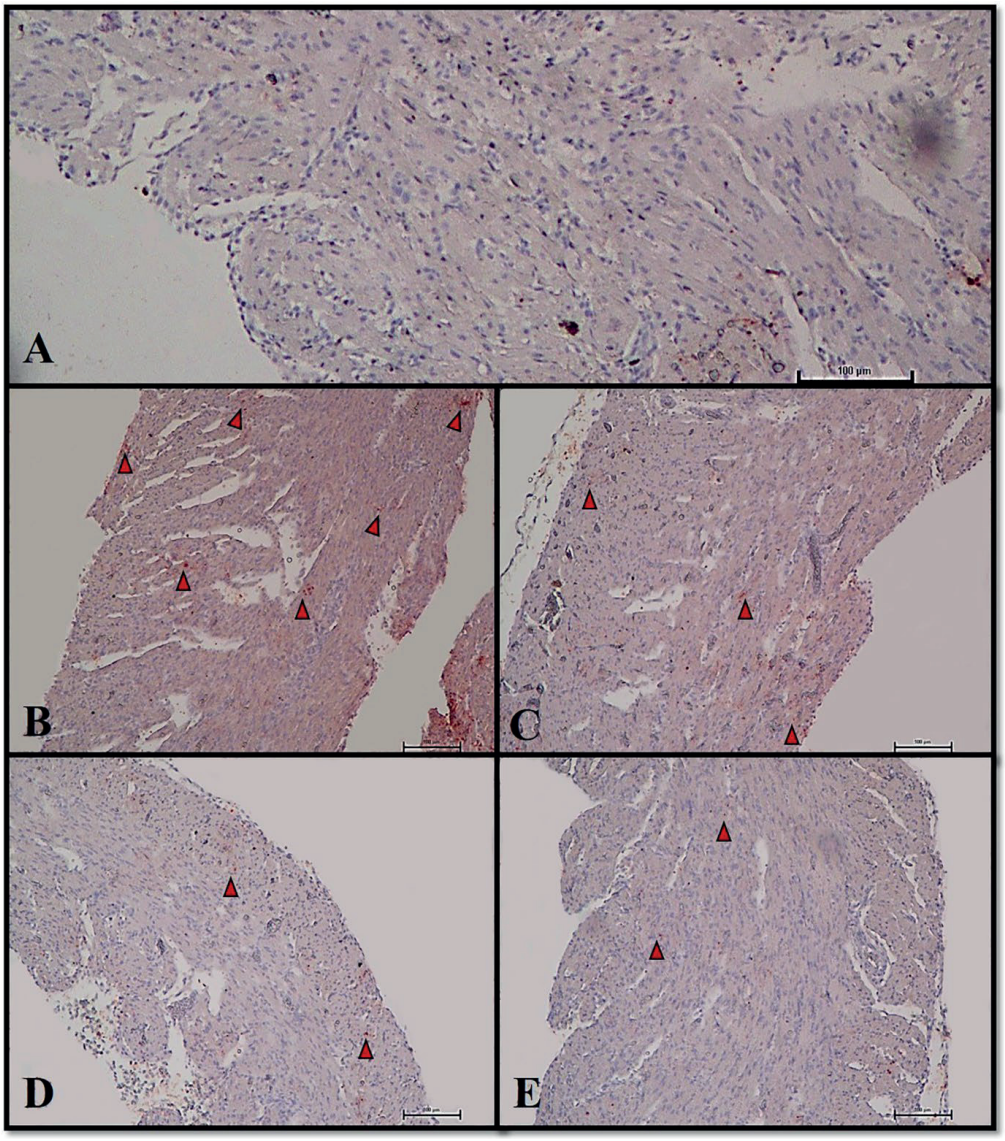

Figure 2. Caspase-3 stained immunohistochemical sections of the experimental groups.
A: Control group, **B:** STZ, **C:** Low dose, **D:** Medium dose, **E:** High dose.

they determined that there was an increase in DNA damage and a decrease in cell migration in mouse embryonic stem cells, which had a negative effect on the formation and development of the heart [22]. Based on this information, it was determined that muscle cells were hypertrophied in direct proportion to glucose consumption and abnormal heart formations were formed. As a matter of fact, in our study, the insulin mechanism was disrupted with STZ administration and sufficient glucose uptake of the heart cells was prevented. Accordingly, the morphometric values of the STZ group embryos were found to be lower than the control group In addition, vitamin K1 was administered as a potential therapeutic in STZ application in our study. An increase in heart morphometry was observed as a result of the administration of vitamin K1. This increase can be explained by the effects of vitamin K1 on pancreatic B cells on insulin secretion (increasing glucose tolerance) and its antioxidant properties that support the regeneration of pancreatic islets and increase insulin secretion [25]. In addition, active caspase-3 expression in diabetic apoptotic cells was also evaluated by immunohistochemical staining method in our study. As a result of the evaluation, it was determined that STZ application increased apoptosis, and vitamin K1 decreased it depending on the rate of vitamin K1 dose.

Similarly, in the literature, Dihinga et al applied olive oil and olive oil + vitamin K1 to type 2 DM mice. It was determined that vitamin K1 decreased basal glucose, insulin levels, body weight in a dose dependent manner compared to the control group [14]. Varsha et al. gave STZ to male Wistar rats for 3 days and attempted to treat them with vitamin K1 (5 mg/kg, twice a week) for 2.5 months. At the end of the study, they determined that vitamin K1 treatment reduced the deaths caused by STZ in endocrine pancreatic cells and vitamin K1 facilitated islet cell regeneration [26]. In other studies in the literature, it has been found that high-dose vitamin K1 intake reduces the risk of new onset type 2 DM [27], and vitamin K1 plays an important role in diabetes induced embryopathy due to its possible roles in various cellular activities such as apoptosis, proliferation and differentiation [22]. In addition, DM triggers oxidative stress that causes tissue pathogenesis, and oxidative stress situmulates the release of reactive oxygen species (ROS). It contributes to apoptosis in ROS under both physiological and pathological conditions. Thus, it is thought that unplanned apoptosis causes cardiomyocyte damage and indirectly causes compensatory hyperplasia of the heart walls through vascular dysplasia. We support the idea that vitamin K1 has an inhibitory effect on ROS due to its antioxidant effect [28], and accordingly, it has a protective/therapeutic effect on the heart wall.

Conclusion

It was concluded in our study that DM is an important factor in cardiovascular diseases and has serious irreversible destructive effects on heart morphometry and histopathology. We have also determined that the therapeutically applied vitamin K1 to DM also reduces the degenerative and hyperplastic effects of DM. However, although we rely on the outcome data of our study, we think that our study should be supported by studies in which the scope is expanded and different doses of vitamin K1 are applied.

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Conflict of interest

Authors declared no conflict of interest.

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Thoracic computed tomography measures have predictive value in the diagnosis of chronic obstructive pulmonary disease

Mustafa Tosun[1] **Edhem Ünver**[1] **Ali Küpeli**[2]

Erdal Karavaş[3] **Sonay Aydın**[4]

1 Department of Chest Diseases, Faculty of Medicine, Erzincan Binali Yıldırım University. Erzincan / Türkiye
2 Department of Radiology, Trabzon Kanuni Training and Research Hospital. Trabzon / Türkiye
3 Department of Radiology, Faculty of Medicine, Bandırma Onyedi Eylül University. Balıkesir / Türkiye
4 Department of Radiology, Faculty of Medicine, Erzincan Binali Yıldırım University. Erzincan / Türkiye

Abstract

Chronic Obstructive Pulmonary Disease (COPD) is diagnosed with pulmonary function tests (PFTs). However, since not all patients can be diagnosed with PFTs, some are diagnosed with radiological or clinical findings. The purpose of this study was to define the properties of obstructive airway disease through thoracic computed tomography (CT) and to identify the diagnostic efficacy of CT findings. A total of 160 patients who underwent PFT and thoracic CT assessment July 2018 - January 2019, were retrospectively analyzed. Based on PFT findings, patients were categorized into three groups as having normal, restrictive or obstructive airways. Age, height, weight, and body mass indexes of the groups were recorded. Pulmonary height, width, right-left hemi-diaphragm height, sterno-diaphragmatic angle and retrosternal transparent area length in axial sections were also recorded. Diagnostic efficacies of these parameters in the detection of obstructive airway disease were measured. Of the 160 patients (109 males, 51 females; mean age = 59.5), 91 (56.9) had normal PFT, 58 (36.2%) had obstructive and 11 (6.9%) had restrictive airway disease. Pulmonary height, width, sterno-diaphragmatic angle, and retrosternal transparent area length were significantly higher in patients with obstructive airway disease while the right-left hemi-diaphragm height was significantly lower (p<0.001). About 60-75% sensitivity and specificity were obtained when identifying the obstructive airway disease with these parameters. These values obtained from the axial and sagittal sections could contribute to the diagnosis of obstructive airway disease.

Keywords: Chronic obstructive pulmonary disease, diagnosis, thorax computed tomography measurements, emphysema

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Corresponding Author:
Erdal Karavaş
Email: erdalkaravas@hotmail.com

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common preventable and treatable disease characterized with airflow restriction and respiratory symptoms arising from airways and/or alveolar anomalies generally induced by serious exposure to harmful particles or gases [1]. COPD is a leading cause of morbidity and mortality worldwide. Its prevalence has increased over years with the increasing exposure to risk factors and the ageing of population [2]. Although findings of COPD is deemed to be irreversible, it has been shown that progression of the disease can be prevented and health outcomes could be improved with early diagnosis.

Presence of symptoms is not always essential for the diagnosis of COPD. Rather, it is important to show exposure to risk factors and airflow restriction with pulmonary function testing (PFT). While chest radiography is the initial radiological inspection in the assessment of patients, it has low specificity and sensitivity values in the diagnosis of COPD (particularly in emphysema) [3].

Today, exposure to radiation has decreased with shortened duration of radiological examinations and it has become easier to assess the prevalence and anatomic distribution of parenchyma, particularly with thoracic computed tomography (CT) [4].

The relationship between the diagnosis of COPD and thoracic CT findings that include air trapping, bronchial wall thickness, tree-in-bud appearance, and thoracic cage ratios, has been identified in several research [5–9]. In this study,

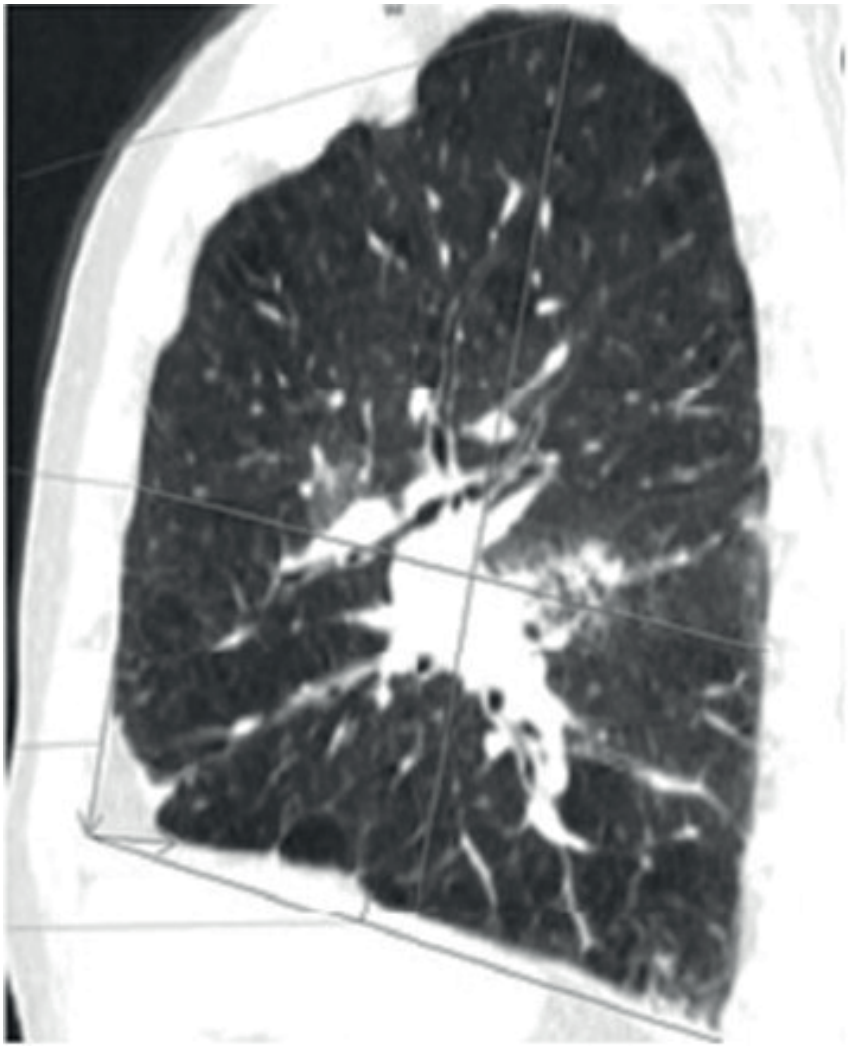

Figure 1. Measurements of pulmonary height, width, right-left hemi-diaphragm height, sterno-diaphragmatic angle in sagittal sections of thoracic CT of a patient with COPD.

we compared the thoracic CT findings of patients with normal PFT compatible with obstruction in order to determine the diagnostic efficacy of CT in COPD.

Materials and Methods

The study protocol was approved by the local Ethics Committee for Clinical Research (2019/04-10).

A total of 160 patients who underwent PFT and thoracic CT July 2018 - January 2019 were assessed retrospectively. PFT values of the patients were evaluated based on the GOLD guide to categorize the patients in 3 groups as having normal, restrictive or obstructive airways. Age, height, weight, and body mass index (BMI) of the groups were recorded.

Acquiring Thoracic CT images:

Images of the patients were acquired with the 16-detector Siemens SOMATOM Sensation 16 (Forchheim, Germany) CT device used in the Radiology Unit *(tube voltage= 120 kV, effective mAs = 90, slice thickness 5 mm, collimation = 2×4 mm, pitch = 1.6).*

Analysing the images:

The measures were taken with Syngo (Siemens Medical Solutions) software at workstation in thoracic CT inspections without notice of PFT

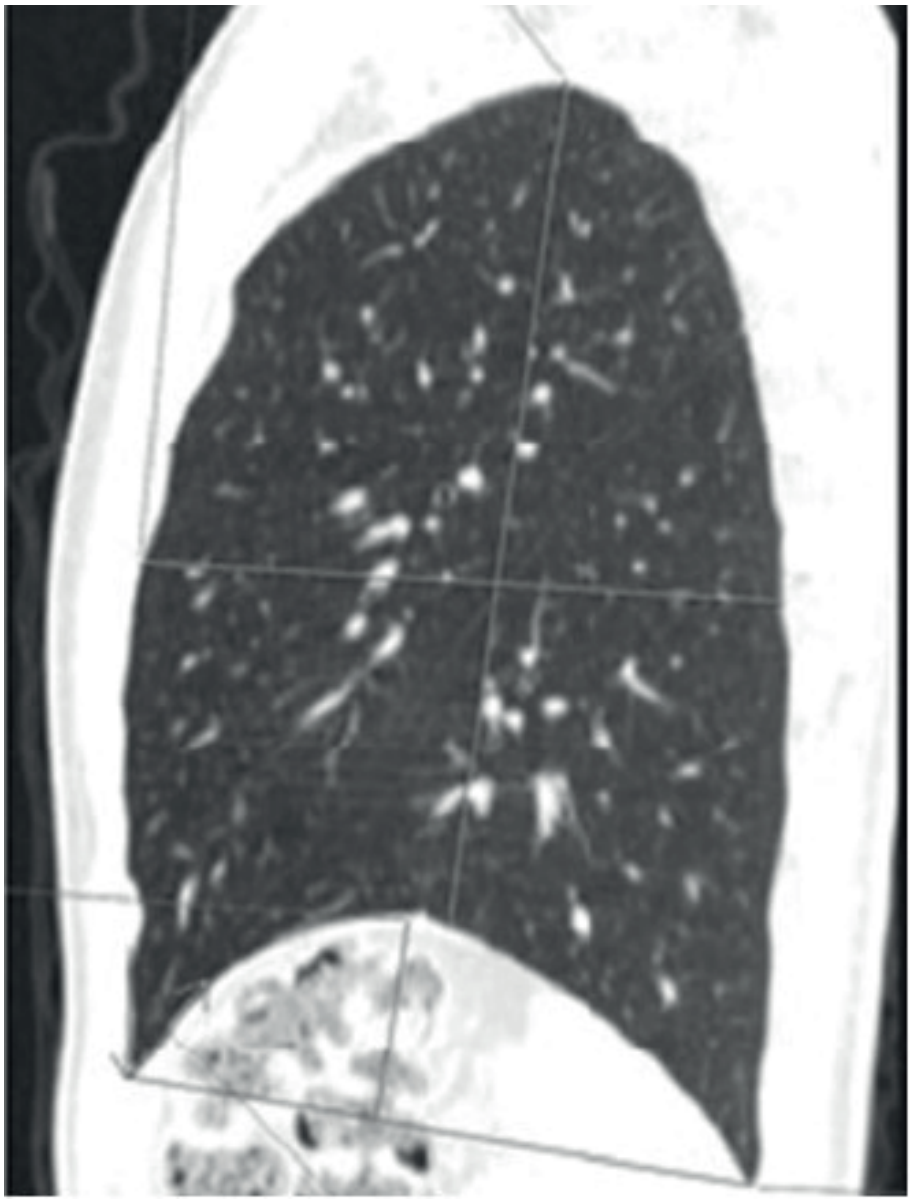

Figure 2. Measurements of pulmonary height, width, right-left hemi-diaphragm height, sterno-diaphragmatic angle in sagittal sections of thoracic CT of a person without COPD.

values upon the consensus of two radiologists with a minimum 5-year experience in the profession.

In sagittal sections;

1. Pulmonary height

2. Pulmonary width

3. Right-left hemi-diaphragm height

4. Stero-diaphragmatic angle measurements were performed (Figure 1,2).

In axial sections, retro-sternal transparent area length was recorded (Figure 3).

Patients with normal PFT testing findings and restrictive pattern and patients with obstructive pattern were compared in terms of these parameters in order to find out their diagnostic efficacy in the detection of obstructive airway disease. Mediastinum and parenchymal windows of the patients were also analyzed to see whether emphysema, bronchiectasis, peribronchial thickening, mucus seal and air trapping were present and the findings were recorded.

Results

Of the 160 patients included in the study, 109 were male and 51 were female. 91 (56.9%) had normal PFT, 58 (36.2%) had obstructive and 11 (6.9%) had restrictive airway disease. Comparison of the demographical data of the patients revealed that the mean age of the patients who had obstructive type of disease was significantly higher than the patients who didn't have such disease (p<0.001). BMI was also significantly higher in the obstructive group compared to the non-obstructive group (p=0.014). There was no significant difference in other demographical data (Table 1).

Compared to the patients with normal and restrictive PFT findings, the group with an obstructive airway disease had significantly higher mean values pulmonary height, width, sterno diaphragmatic angle, and retrosternal transparent area length while the group's mean right-left hemidiaphragm height was statistically significantly lower (p<0.001, Table 2).

About 60-75% sensitivity and specificity were obtained when identifying the obstructive

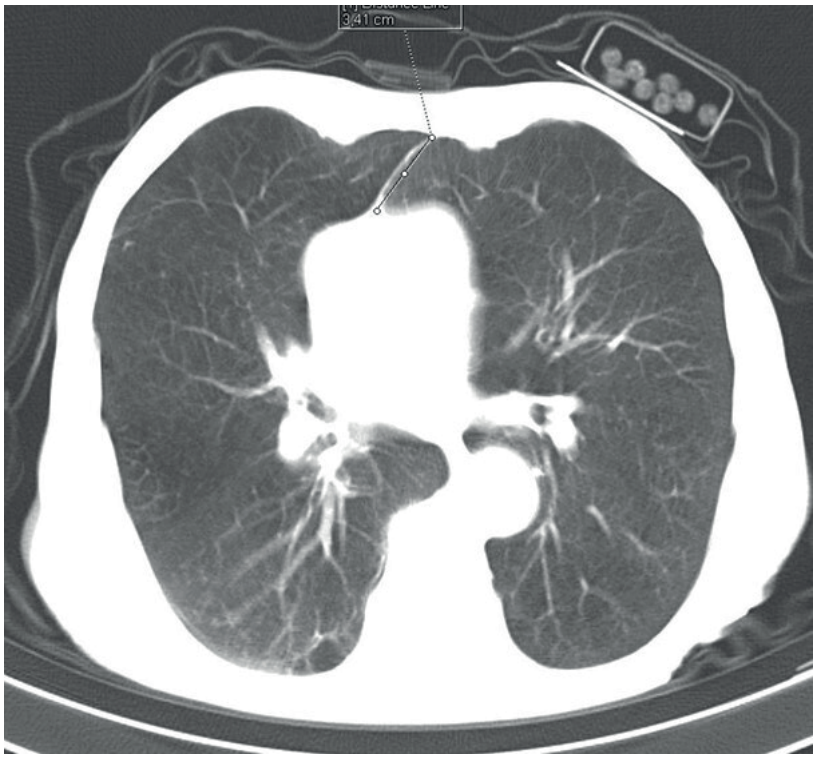

Figure 3. Retro-sternal transparent area length measurement in axial section.

airway disease with these parameters.

Parenchymal and mediastinal analysis revealed emphysema in 33 patients (20.6%). 22 of these patients were in the obstructive group (p<0.001). Among other findings, bronchiectasis was found in 21 patients (13.1%). 14 of these patients were in the obstructive group (p=0.002). Similar to emphysema, the ratio of patients diagnosed with peribronchial thickening (31.3%), air trapping (40%) and mucus seal (15%) was significantly higher in the obstructive group (p<0.001, Table 3).

While the highest sensitivity was found with pulmonary height (74.1%) and pulmonary width in ROC (Receiver Operating Characteristic) analysis, the highest specificity was found with the right hemidiaphragm height with a rate of 67.6%. Positive predictive values (PPV) of the findings were close to each other with a mean rate of 53%. When negative predictive values (NPV) were studied, they were measured around 80% in all findings, with the left hemidiaphragm had the highest value (81.9%). Besides, under the curve areas of these parameters, i.e. AUC values were between 0.690-0.739 and comparison of AUCs did not reveal any statistically significant difference (p=0.241). All ROC analysis findings are shown in Figure 4 and Table 4.

Table 1. Demographical features of the patients.

	Total	Obstructive Airway Disease		*p* value
		Yes	No	
Number	160	58	102	
Age	50.4 ± 14 (23-90)	64.3 ± 9 (44-88)	56.7 ± 14 (31-87)	<0.001
Sex Male				<0.002
Male	109	48	61	
Female	51	10	41	
Height (cm)	167.4 ± 8.7 (150-195)	163.8 ± 7.6 (145-178)	162.4 ± 10.4 (137–192)	0.397
Weight (kg)	83.4 ± 11.9 (53-140)	75.0 ± 15.1 (64.5-108)	79.9 ± 16.9 (51-137)	0.067
BMI	29.5 ± 6.2 (18.9–55.68)	30.4+ 6.6 (18.9-55.8)	27.9 ± 52 (19.2-44.3)	0.014

Abbreviations: BMI = Body mass index.

Table 2. Comparison of the parameters measured with thoracic CT.

	Total	Obstructive Airway Disease		*p* value
		Yes	No	
Number	160	58	102	
Pulmonary height	19.6 ± 2.9 (11.7-26)	21 ± 26 (13.7-26)	18.8 ± 2.8 (11.7-23.8)	<0.001
Pulmonary width	18.3 ± 19 (14.5-23.7)	19.4 ± 1.8 (14.5-23.7)	17.7 ± 1.7 (14.7-23)	<0.001
R hemi. height	37 ± 12.2 (8-71)	30.6 ± 14.1 (8-67)	40.7 ± 9.2 (19-71)	<0.001
L hemi height	31 ± 11.3 (7-67)	25 ± 11.9 (7-57)	34.5 ± 9.4 (11-67)	<0.001
R sterno. angle	63.2 ± 16.6 (26-169)	68.8 ± 15.5 (26-96)	60 ± 16.4 (30-169)	0.001
L sterno. angle	68.3 ± 16.9 (28-145)	74.3 ± 16.8 (28-96)	64.9 ± 16.1 (31-145)	0.001
R sterno. angle	10.6 ± 6.7 (4-46)	14.9 ± 8.3 (4-46)	8.1 ± 3.3 (4-20)	<0.001

Abbreviations: Hemi = hemidiaphragm; sterno= sterno-diaphragmatic.

Discussion

COPD is a leading health issue in terms of mortality, morbidity, and economic losses today. While investigation of new drugs and methods for the treatment of the disease continues, methods to be used in early diagnosis of the disease are under development. Early diagnosis and treatment are two major factors affecting the prognosis of the disease [2,3]. Being non-invasive, inexpensive and easily applicable in monitoring of the treatment, pulmonary function tests (PFTs) are among the main methods used in the diagnosis of COPD. So, they are primarily preferred in the phasing of the disease [3]. While

Table 3. Comparison of the findings obtained from the mediastinum and parenchymal window images of the patients.

	Total	Obstructive Airway Disease		*p* value
		Yes	No	
Emphysema				<0.001
Yes	33	22	11	
No	127	36	91	
Bronchiectasis				0.002
Yes	21	14	7	
No	139	44	95	
Peribronchial Thick.				<0.001
Yes	50	30	20	
No	110	28	82	
Air Trapping				< 0.001
Yes	64	37	27	
No	96	19	75	
Mucus Seal				<0.001
Yes	24	20	4	
No	136	38	98	

Abbreviations: Thick = thickening.

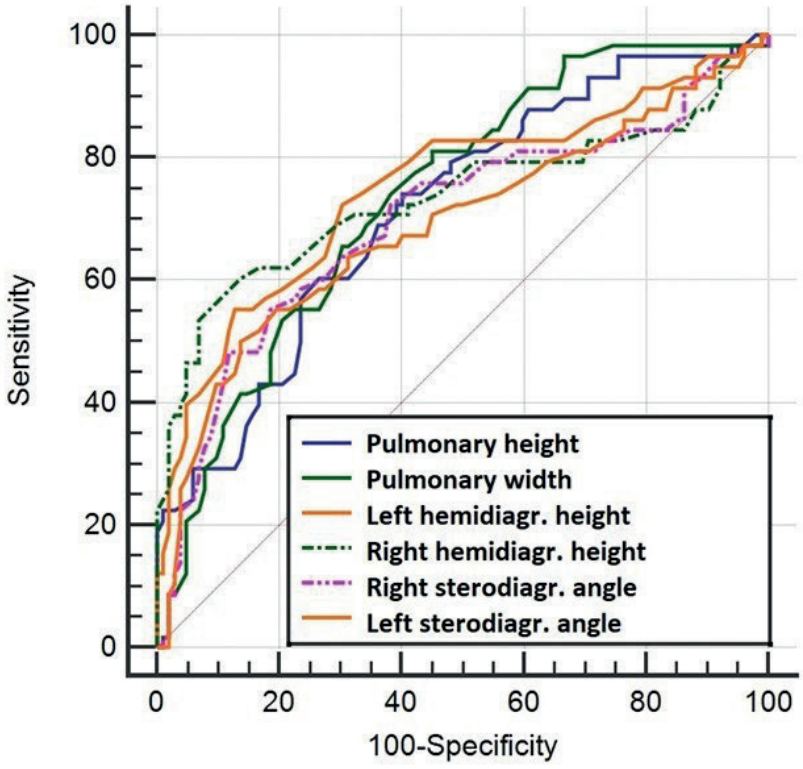

Figure 4. ROC analysis graphics.

PFT is deemed to be the gold standard, it has been suggested in a study that its rate of accuracy in the detection of the disease is between 62-64% when PFT values are considered together with clinical findings according to ATS and ERS guidelines [10]. While chest radiography is significant in the detection of additional parenchymal pathologies such as pneumonia, solitary pulmonary nodule, and pulmonary embolism, it is a method with low specificity and sensitivity in the diagnosis of COPD (particularly in emphysema) [11]. However, chest radiography will be a useful and primarily preferred method particularly in the differential diagnosis of COPD exacerbation, heart failure or acute pathologies like pneumothorax [12]. Vascular changes and hyperinflation are the most important indicators in chest radiography. The most radiologically reliable indicator of hyperinflation is the flattening of the diaphragm. This finding is also correlated with the degree of narrowing in airways [13,14].

Retro-sternal area above 2.5 cm, a pulmonary height >30 cm, long and narrow heart shape and enlarged costophrenic angle also support the presence of emphysema [15]. Despite all these, chest radiography is basically a method supporting diagnosis rather than being a diagnostic method. Thoracic CT is a method that is much more sensitive and specific than standard chest radiography [16–18]. Two basic methods as the visual method and quantitative assessment are used for the diagnosis of emphysema in CT. Correlation between visual assessment and histopathological assessment of emphysema has been shown by several studies in previous years [19–21]. There are also studies in which the detection of emphysema by quantitative CT is associated with PFT [22,23].

Sakai et al., carried out a study based on these criteria, where they used the observation method based on the prevalence and severity of emphysema and showed that there was a strong correlation between visual scoring values and PFT [24]. However, visual assessment has some disadvantages like subjectivity and the effects of observer's experience and different window settings on interpretation [25]. Thoracic CT and quantitative assessment are in parallel with technological developments. In a study conducted by Nakano et al. on 114 smokers, it was showed that there was a correlation between the right lung upper lobe segment bronchial diameter thickness and the narrowing in airways

Table 4. ROC analysis findings.

	AUC	Threshold Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Pulmonary height	0.717	19.6	74.1	59.8	51.2	80.3
Pulmonary width	0.736	18.3	74.1	61.7	52.4	80.8
R hemi. height	0.735	36	70.6	67.6	55.2	80.2
L hemi. height	0.749	31	74.1	66.6	55.8	81.9
R sterno. angle	0.699	62	72.4	61.7	51.9	79.9
L sterno. angle	0.690	69	65.5	63.7	50.7	76.5
Retro-sternal transparent a.	0.739	8	68.9	64.7	52.6	78.6

Abbreviations: Hemi = hemidiaphragm; sterno = sterno-diaphragmatic; a = area.

[26]. In another study, by examining thoracic CT scans taken for lung cancer screening, patients were evaluated for COPD and concluded that inspiratory thoracic CT biomarkers alone may be sufficient to identify patients with COPD [18].

In a study conducted by Hightower et al., PFT-diagnosed obstruction was found to be significantly correlated with sterno diaphragmatic angle and hemidiaphragm assessment among the quantitative assessments [27]. In the same study comparing the qualitative and quantitative measurements with regards to their demonstration of the presence of obstruction, specificity of qualitative measurements was over 90% while it changed between 80-90% in quantitative measurements. On the other hand, sensitivity was not high in either measurement [27]. Unlike that study, we found that pulmonary height and pulmonary width had the highest sensitivity with a rate of 74.1%, and right hemidiaphragm height had the highest specificity with a rate of 67.6%.

Mild and moderate emphysema cases are relatively asymptomatic. There is a mild difficulty in breathing in these patients yet coughing and phlegm are less than chronic bronchitis. Therefore, patients underestimate these symptoms and most of them spend many years without presenting to a hospital. Hence, early diagnosis rate of the disease decreases [24,28,29]. PFT cannot directly reveal emphysema when measuring pulmonary volumes, flow rates and the severity of obstruction. While many parameters in PFT reflect airway obstruction, they cannot show the parenchymal loss caused by emphysema. PFT can even display normal findings in the presence of the disease [24,30]. In a study evaluating the contribution of emphysema, air trapping and airway wall thickness measured by CT to lung functions, it was determined that each measurement contributed to a different PFT parameter [31]. In our study, thoracic CT findings of 33 of the 160 patients revealed emphysema. PFT of 2/3 of these 33 patients were obstructive (p<0.001). However, there were 11 more patients with normal PFT yet emphysema in thoracic CT. This showed that we could use thoracic CT to reveal the presence of emphysema in patients prior to the disruption of values in PFT. Indeed, thoracic CT has been reported to be the most effective method in the diagnosis of emphysema [22,32,33]. In a study conducted by Lakadamyali et al., patients underwent high resolution computed tomography (HRCT) to find out whether emphysema as a finding of COPD was present or not; and findings such as bronchiectasis, peribronchial thickening, air trapping and mucus seal were not included in the study [12]. In our study, all above-mentioned findings including emphysema were found to be significantly higher in the obstructive group.

Conclusion

In conclusion, early diagnosis and treatment of COPD is important for the reduction of mortality, morbidity, and treatment expenses. As obstructive changes do not occur in early stage in PFT, thoracic CT assessment of patients with suspected clinical findings could be helpful in early diagnosis. Although the high cost of PFT makes it difficult to be requested for each patient, we consider it to be advantageous in the reduction of annual loss of FEV1 as the diagnosed person will quit smoking and receive treatment. PFT could also be helpful in the detection of other findings that might be added to COPD.

Limitations: The main limitations of our study are its retrospective nature and the relatively small number of patients. In addition, although HRCT was generally used in previous similar studies, we used thorax CT and we did not take inspiration-expiratory measurements.

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Conflict of interest

The authors declare that they have no conflict of interest.

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ORIGINAL ARTICLE

The evaluation level of acute trauma pathologies by the emergency medicine physician assistant in abdominal computed tomography images of the trauma patients

Mehmet Soyugüzel[1] **Ayşe Ertekin**[1] **Esra Özgül**[2]

1 Department of Emergency Medicine, Faculty of Medicine, Afyonkarahisar Health Sciences University. Afyonkarahisar / Türkiye
2 Department of Radiology, Faculty of Medicine, Afyonkarahisar Health Sciences University. Afyonkarahisar / Türkiye

Abstract

Abdominal injury is the third leading cause of death due to trauma. In this study, it is aimed to investigate the level of detection of acute trauma pathologies by the emergency medicine physician assistant in abdominal tomography images taken in trauma patients. Contrast-enhanced abdominal tomography images of 207 patients who applied with trauma between 12.15.2020 and 12.15.2021 were included in this study. In order to evaluate the images of the patients, the evaluation of the emergency medicine physician assistant was compared with the radiology official report. Patients' age, gender, current complaints, symptoms, trauma classification, injury sites accompanying abdominal injury, hospitalization status and mortality rates were analyzed. The statistical distribution of the patients' demographic and clinical information was calculated. The reports of the patients whose radiology official report was issued and the emergency medicine assistant forms were transferred to the SPSS program as "pathology exists" or "no pathology". In the study, 79.2% (n=164) were male and 20.8% (n=43) were female. The median age was 33 years. In terms of interpretation of abdominal tomography, a statistically significant correlation was found between the radiologist and the emergency medicine physician assistant in the evaluation of liver, spleen and kidney; intra-abdominal and retroperitoneal hemorrhage, muscle and fascia injury of abdominal wall; vertebral, iliac, ischiatic, pubic bone, sacrum and femoral neck fracture. It was determined that 12.1% (n=25) of the patients were admitted to the intensive care unit and 5.3% (n=11) were died. High sensitivity, specificity, positive and negative predictive values were found in the evaluation of abdominal contrast-enhanced tomography imaging of patients admitted to the emergency department due to trauma by the emergency medicine assistant. We think that these high accuracy values are due to emergency medicine physician assistant's evaluation of the patient's history, physical examination and imaging studies as a whole.

Keywords: Trauma, abdominal computed tomography, emergency medicine physician assistant, emergency department

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Corresponding Author:
Ayşe Ertekin
Email: doktorayse6@yahoo.com

Introduction

Trauma causes 10% of deaths worldwide. Trauma is among the leading causes of death between the ages of 1-45 in the United States [1]. Abdominal injury, it ranks third among the causes of death due to trauma after head, neck and thorax injuries [2]. Causes of abdominal injury include in-vehicle and out-vehicle traffic accidents, sharps and stab wounds, work accidents, assault and falling from a height [1]. Computed tomography (CT) is the most accurate non-surgical diagnostic method of the extent and anatomy of the injury in trauma patients [3]. It is life-saving for the patient when the emergency medicine assistant (EMPA), who sees the patient for the first time, evaluates the abdominal CT and makes the necessary intervention by clinical correlation. Because knowing the clinical correlation is much more helpful when interpreting CT images [4]. Although evaluating abdominal CT images is critical, there are not enough studies on the comparison of abdominal CT evaluation of emergency medicine workers with the radiology official report. In this study, we aimed to investigate the correct diagnosis rate of the EMPA in the evaluation of acute trauma pathologies in abdominal CT and to see how compatible it is with the official radiology reports, thus avoiding incomplete or misinterpretations.

Materials and Methods

Ethical aspect of the research

This study was approved by the Ethical Committee of Afyonkarahisar Health Science University (2020/554). Written informed consent was obtained from the patients/relatives evaluated within the scope of the study, by informing them about the subject of the study.

Designing of the research

We evaluated 207 patients who applied to Afyonkarahisar Health Sciences University Medical Faculty of ED with trauma and underwent abdominal CT between 15.12.2020 and 15.12.2021 were evaluated prospectively. Trauma patients who underwent non-contract abdominal CT and patients over 90 years of age were not included in our study. To evaluate the images of the patients, EMPA who completed three years and completed the radiology rotation was selected. Contrast-enhanced abdominal CT was evaluated by EMPA and compared with the radiology official report. The correct diagnosis rate of EMPA was examined. EMPA was blind to the radiology report when interpreting the images. The Picture Archiving and Communication Systems (PACS) system in the emergency department (ED) was used for evaluating abdominal CT images. Radiology report was followed from Nucleus hospital information management system. All of the CT images were evaluated by the same 15-year experienced specialist abdominal radiologist. The radiologist's report was accepted as the gold standard. In addition, patients' age, gender, current complaint, symptoms, trauma classification (such as in-vehicle and/or out-of-vehicle traffic accident, falling from a height, beating, gunshot wounds, stab wounds), injury areas accompanying abdominal injury, hospitalization status and mortality rates were examined. The statistical distribution of the patients' demographic and clinical information was calculated. The reports and EMPA forms of the patients whose radiology official report was issued were transferred to the Statistical Package for the Social Sciences (SPSS) program as "pathology exists" or "no pathology". The evaluations made by EMPA and the official radiology report as "pathology exists" or "no pathology" were accepted as valid and compatible. Differently, "pathology exists" or "no pathology" in the EMPA and the official radiology report was accepted as incompatible.

CT protocol

Abdominal MDCT examinations were performed by a CT scanner (Toshiba Aquilion (80x2), Otawara, Japan). The patients were given 1-2 ml/kg iodinated nonionic contrast agent with an iodine concentration of 300 mg/cc. CT images were obtained during patient breath holding using the following parameters: slice thickness 2 mm, reconstruction index 1 mm, tube voltage 120 kVp, pitch 0.75. Slices were extended from diaphragmatic dome to the end of pelvis. Coronal and sagittal multiplanar reconstructed (MPR) images were obtained from axial CT images.

Statistical analysis method

In the analysis of the data, categorical variables were presented as percent (%) and frequencies. Age, which was a continuous variable, was expressed as the median (minimum-maximum value). Chi-square test was used for comparison of categorical variables between groups. The compatibility between the evaluations of the radiologist and EMPA was evaluated with the Cohen kappa correlation. Kappa coefficient (Ƙ) was obtained to examine the level of concurrence. The results of Kappa concordance analysis were presented as significance level p and concordance power Ƙ. Statistical analyzes were done with SPSS 26.0 package program. All the *p* values presented were bidirectional and the values with $p<0.05$ were expressed as statistically significant.

Results

Of the 207 patients in the study group, 79.2% (n=164) were male and 20.8% (n=43) were female. The median age of the patients was 33 years (1-89).

Trauma mechanisms were; 58.5% (n= 121) in-vehicle traffic accident, 15.5% (n= 32) out-vehicle traffic accident, 15.5% (n=32) falling, 3.9% (n=8) penetrating injury, and 0.5% (n=1) blunt injury. However, 6.3% (n=13) of the patients were injured by other mechanisms (explosive material, heat and barotrauma injuries).

In addition, when evaluated, it was determined that 38.6% (n=80) of trauma patients who underwent abdominal CT had no additional abdominal injury. However, 10.6% (n=22) of the patients had limb fracture, 10.1% (n=21) cranial injury (including intracranial fractures, intracranial hemorrhages and contusions), 7.7%

Table 1. Pathological lesion evaluation of the emergency medicine physician assistant and the radiologist.

Pathological Lesion	Lesions that EMPA and Radiologist jointly detected pathology		Lesions that EMPA and Radiologist detected pathologies differently		*p*	Ƙ
	Number of patients jointly detected as Pathology Exists	Number of patients jointly detected as No Pathology	Number of patients in whom Pathology Exists and EMPA detected No Pathology	Number of patients No Pathology and in whom EMPA detected Pathology Exists		
Liver injury	6	192	6	3	**<0.001**	0.549
Spleen injury	4	198	2	3	**<0.001**	0.603
Kidney injury	2	204	1	0	**<0.001**	0.798
Adrenal injury	0	202	3	2	**0.863**	-0.012
Pancreatic injury	0	206	1	0	**1.000**	0.001
Intraabdominal hemorrhage	17	186	3	1	**<0.001**	0.884
Retroperitoneal hemorrhage	3	204	0	0	**<0.001**	1.000
Muscle injury of the anterior-posterior wall of the abdomen	4	201	1	1	**<0.001**	0.795
Fascia injury of the anterior-posterior abdominal wall	4	202	0	1	**<0.001**	0.886
Vertebral fracture	26	175	4	2	**<0.001**	0.880
İliac fracture	8	199	0	0	**<0.001**	1.000
Ischiatic fracture	9	197	1	0	**<0.001**	0.945
Pubic bone fracture	13	193	0	1	**<0.001**	0.960
Sacrum fracture	3	203	1	0	**<0.001**	0.855
Femoral neck fracture	3	204	0	200	**<0.001**	1.000

EMPA: Emergency Medicine Physician Assistant, Ƙ: Kappa coefficient

(n=16) vertebral injury, 3.4% (n=7) had thoracic injuries, 2.9% (n=6) pelvis and femur neck fractures, 4.3% (n=9) other sites (genital, scrotum, scalp lacerations and facial bone fractures) injuries were found. In addition, 22.2% of our patients (n=46) had additional injuries in more than one region. Abdominal injury was detected in 6.25% of the patients (n=46) without additional injury. 60% of patients with abdominal injuries had abdominal pain.

In this study, intra-abdominal injury was determined in 33 (15.9%). Intra-abdominal injury was detected in 2 (25%) of 8 patients with penetrating injuries, 7 (21.9%) of 32 patients with out-vehicle traffic accidents, 6 (18.8%) of 32 patients with fall injuries, 18 (14.9%) of 121 patients with in-vehicle traffic accident. There was no difference between injury mechanisms and intra-abdominal injury rates (p=0.51).

It was determined that 77.8% (n=161) of 207 patients could not describe their abdominal pain. While 11.1% (n=23) of the patients had abdominal pain, it was determined that the abdominal pain was uncertain in 11.1% (n=23) of the remaining patients due to reasons such as the patient's inability to express himself/herself due to his/her age and not being evaluated due to intubation.

In the study, no agreement was found between the radiologist and EMPA in the evaluation of adrenal and pancreatic injuries of the patients. A statistically significant agreement was found between the radiologist and EMPA in liver, spleen, kidney injury, intra-abdominal, and retroperitoneal hemorrhage detection, detection of muscle and fascia injury in the anterior and posterior abdominal wall, vertebral, iliac, ischiatic, pubic bones, sacrum fracture and femoral neck fracture evaluations (Table 1).

The findings of the study showed that EMPA was able to detect the highest rate of pathological lesions with 100% sensitivity for retroperitoneal hemorrhage, fascia injury in the anterior and posterior abdominal wall, iliac, ischiatic, pubic bone and femoral neck. EMPA estimated with 100% specificity for kidney and pancreatic injury, retroperitoneal hemorrhage, fracture of iliac, ischiatic bone, sacrum and femoral neck. There was no case where the specificity of EMPA to detect pathological lesions was low (lowest specificity was detected for liver injuries with 97%). In this study, the highest positive predictive value (PPV) of EMPA with 100% was determined for kidney injury, retroperitoneal hemorrhage, fracture of iliac, ischiatic bone, sacrum and femoral neck. The lowest PPV was 0% for adrenal and pancreatic injuries. While the highest negative predictive value (NPV) was found for 100% retroperitoneal hemorrhage,

Table 2. The sensitivity, specificity, positive predictive value and negative predictive value of emergency medicine physician assistant to detect lesions by pathology types.

Pathological Lesion	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Liver injury	50	97	66.6	96.9
Spleen injury	66.7	99	57.1	99
Kidney injury	66.7	100	100	99.5
Adrenal injury	0	99	0	98.5
Pancreatic injury	0	100	0	99.5
Intraabdominal hemorrhage	85	99.5	94.4	98.4
Retroperitoneal hemorrhage	100	100	100	100
Muscle injury of the anterior-posterior wall of the abdomen	80	99.5	80	99.5
Fascia injury of the anterior-posterior abdominal wall	100	99.5	80	100
Vertebral fracture	86.7	98.9	92.9	97.8
Iliac bone fracture	100	100	100	100
Ischiatic bone fracture	100	100	100	100
Pubic bone fracture	100	99.5	92.9	100
Sacrum fracture	75	100	100	99.5
Femoral neck fracture	100	100	100	100

PPV: positive predictive value, NPV: negative predictive value

fascia injury in the anterior and posterior abdominal wall, fracture of iliac, ischiatic, pubic bones and femoral neck, there was no pathological lesion with low NPV of EMPA (the lowest NPV was 96.9% belonged to the detection of liver injury), (Table 2).

Considering the final status of the trauma patients who underwent abdominal CT, 58.9% (n=122) were discharged, 21.3% (n=44) were admitted to the service, 12.1% (n=25) were admitted to intensive care, 5.3% (n=11) died, 1.4% (n=3) were discharged with rejection of the treatment, and 1% (n=2) were referred to another institution. CT

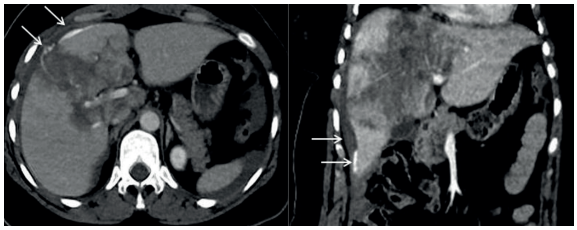

Figure 1. Liver injury. In contrast-enhanced axial and coronal CT, laceration and vascular injury covering more than 75% of the lobe, contrast medium extravasation consistent with active bleeding, and perihepatic hemorrhagic free fluid (arrows) are

Figure 2. Spleen and kidney injury. In contrast-enhanced axial CT, a laceration area (white arrow) is observed in the spleen parenchyma. In addition, left kidney injury and accompanying perirenal hematoma (dashed arrow) are seen.

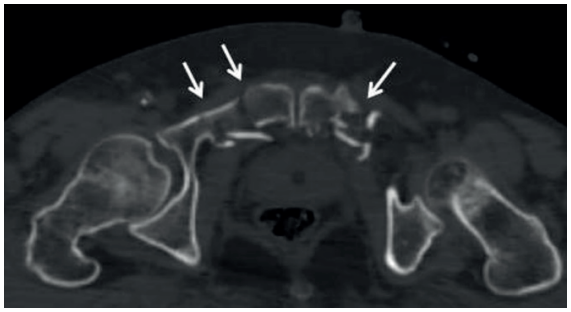

Figure 3. Pubic bone injury. At bone dose, axial CT

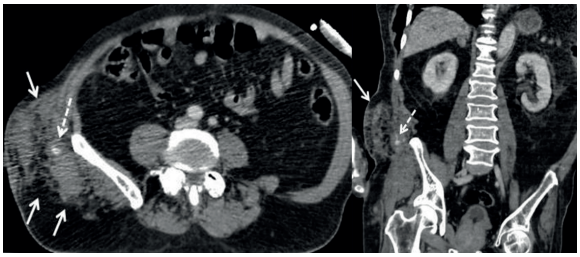

Figure 4. Muscle injury of the posterior-lateral wall of the abdomen. Axial (A) and coronal (B) CT images with IV contrast show hemorrhage in the right abdominal lateral wall and gluteal muscles (arrows)

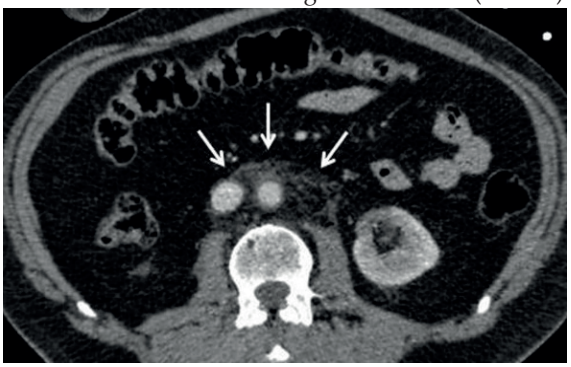

Figure 5. Retroperitoneal injury. In the axial CT image with IV contrast, density increases consistent with retroperitoneal hemorrhage in the paraaortic area were seen (arrow).

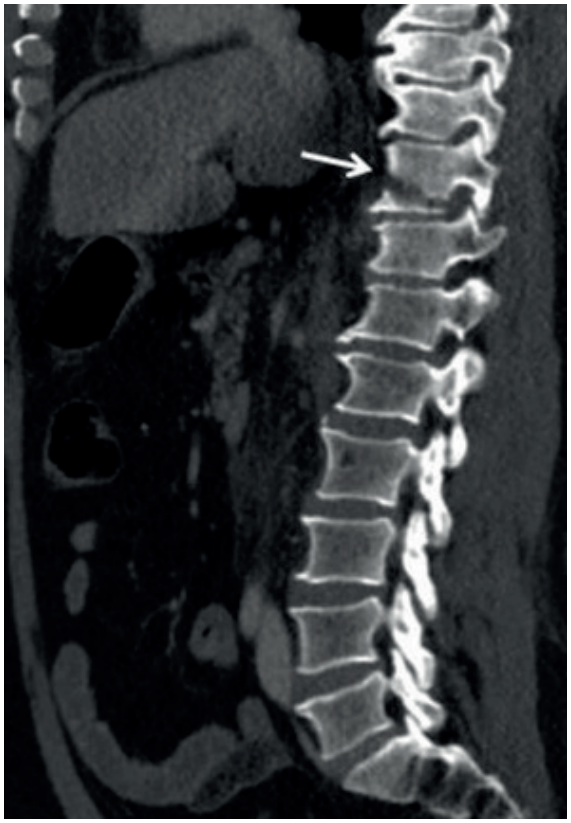

Figure 6. Vertebral injury. A vertical fracture line is observed in the T10 vertebral body in the sagittal CT image (arrow).

Discussion

In order to reduce mortality in stable trauma patients, it is essential to quickly detect acute pathologies with CT and perform the necessary intervention. Since hemorrhagic shock can develop within minutes in trauma patients, it is vital for the emergency physician to see the acute pathology in the CT before the radiology interpretation and take the necessary intervention [5].

In a study, it was reported that 77% of trauma patients were male, 23% were female, and the median age was 39 (26-54) [6]. In another study, it was reported that the incidence of abdominal trauma was higher in young men [7]. Similarly, in our study, abdominal CT was performed in a total of 207 patients, of whom 79.2% (n= 164) were male and 20.8% (n= 43) were female. However, the median age of the patients was 33 years (1-89) in our study. Also, this median age of trauma correlates with American data. Because it is the leading cause of death in trauma between the ages of 1-45 [1].

In a study conducted by Güven et al. including patients of falling from a height (49.1%) and traffic accidents (43.5%) were the most common reasons for trauma patients to apply to the ED, followed by stabbing (2.9%), firearm injuries (2.3%) and other injuries (2.3%) [6]. In our study, similar to the literature, it was determined that of the trauma patients who applied to the ED and required abdominal CT, 58.5% had an in-vehicle and 15.5% had an out-vehicle traffic accident. These data were in accordance with the Turkish Statistical Institute's data on all in-vehicle (50.4%) and out-of-vehicle traffic (motorcycle accident-18.8%) accidents in Türkiye [8]. In addition, according to the data of the World Health Organization, men involved in traffic accidents were found to be three times higher than women, as in our study, and this was in conformity with our study [9]. In our study, all of them were categorized separately without generalization, and no significant difference was found between injury mechanisms and intra-abdominal injury rates. The reason for this was predicted as the severity of the injury rather than the mechanism of the injury and the insufficient number of cases.

Abdominal pain was not present in 40% of patients with abdominal injuries without additional injuries. This showed us that patients can have abdominal injury without no additional injury and abdominal pain. In order to determine this, it is vital for the emergency physician to evaluate the patient with clinical correlation, anamnesis and physical examination [10].

In a study designed by Vaziri et al. the results of abdomino-pelvic CT scans of patients admitted to ED with abdomino-pelvic trauma, a high agreement value (κ= 0.881) was found between interpretation of emergency medicine physicians and radiology physicians [7]. Similarly, in our study, a statistically significant agreement was found between interpretation of EMPA and the radiologist.

In a study conducted with 156 patients with multiple injuries who were over the age of 18

who underwent CT scan, similar to our study, emergency room physicians and on-duty radiologists were compared [11]. In our study, PPD values for liver injury and spleen injury was showed similarity to the study. In a study designed by Vaziri et al. found the sensitivity, specificity, PPD and NPD values of emergency room doctor reports in terms of spleen hematoma were found to be 86.67%, 99.56%, 81.25%, 99.71% and Kappa coefficient 0.836% [7]. In our study, it was determined that the sensitivity, specificity, PPD and NPD values of EMPA to detect spleen lesions were similar to the study of Vaziri et al.

In a study conducted by Güven et al., the official report of emergency medicine physicians and radiology was compared for the interpretation of abdominal CT performed on 232 trauma patients [6]. When liver injury and spleen injury were evaluated, our study had similar sensitivity, specificity, and NPD values with the study of Güven et al. However, compared to our study of spleen and liver injury, higher PPD values were found in the study of Güven et al.

In a study conducted by Kartal et al. bleeding was not classified as intra-abdominal or retroperitoneal hemorrhage and was accepted as abdominal hemorrhage. And also, in a study designed by Güven et al. and Kartal et al. the pelvic fracture was evaluated as a whole [6,11]. In our study, EMPA had higher sensitivity, specificity, PPD and NPD values in detecting kidney injury, intra-abdominal hemorrhage, and pelvic fractures compared to the study of Güven et al. In our study, intraabdominal and retroperitoneal hemorrhage were evaluated separately.

However, in our study, unlike similar studies, the pelvis bone was evaluated in 3 parts as iliac, ischiatic and pubic bone. As a result of our study, the PPD value of the pubic bone was found to be lower than that of the iliac and ischial bones. The sensitivity, specificity, PPD, and NPD value of EMPA were found to be 100% accurate for pathology detection in iliac and ischiatic bone. Our study is a rare and valuable study in terms of dissecting and examining the pelvis bone and obtaining meaningful results. In addition, the existence of different results detected in our study was explained that there was only one EMPA in the study and the difference in the number of cases.

In our study, femoral neck fracture was evaluated by EMPA. A 100% agreement was found in terms of sensitivity, specificity, PPD, and NPD. These statistics are not available in the studies. In addition, unlike other studies, vertebral fractures were detected in 26 patients in our study, and a statistically significant agreement was found between the radiologist and EMPA in the fracture evaluations [6,11]. Also, muscle and fascia injury in the anterior and posterior abdominal wall was evaluated in our study and it was found to be statistically significant. Our study is also a rare and valuable study in this respect.

In a study designed by Bagheri et al., the effect of contrast-enhanced CT interpretation on morbidity and mortality by emergency medicine physicians was investigated. In the study, it was seen that 68.2% of the abdominal CT interpretations of emergency medicine physicians were interpreted correctly. In the study, 5 patients died, and no preventable cause was found by early CT interpretation in any patient [12]. Our study was not categorized as preventable or unavoidable causes. Compared to the study by Bagheri et al., our study had higher accuracy rate. This difference was explained by the fact that our study was conducted on a single EMPA, the lack of official radiology training in the study of Bagheri et al., and the difference in the number of cases.

In our study, whole body CT scanning was performed in 90% or more of trauma patients. In a study by Tillou et al., 284 patients with blunt trauma were evaluated and it was reported that whole body CT scan was unnecessary at a rate of 27%. It was found that the injury would have been missed in two patients who required immediate intervention had the whole-body CT scan not been performed. It was also found that potentially significant injuries would be missed in 17% of total patients [13]. Of the 207 patients included in our study, 122 were discharged. If the discharged patients are considered clinically insignificant, it is concluded that CT performed in 58% of trauma patients is unnecessary. This is

due to the increase in malpractice cases and the possibility of abdominal injury despite clinical incompatibility.

Conclusion

High sensitivity, specificity, PPV and NPV were found in the evaluation of abdominal contrast-enhanced CT imaging of patients admitted to the ED due to trauma by the EMPA. We think that these high accuracy values are due to EMPA's evaluation of the patient's history, physical examination and imaging studies as a whole.

Study limitations

In our study, abdominal CT evaluation was performed by a single EMPA. Great vessel injuries and mesenteric contusion were not included in our study. Additionally, intra-abdominal injuries were evaluated as "pathology exists" or "no pathology", and the grading the injury level of solid organs were not specified.

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Conflict of interest

There are no conflicts of interest to declare.

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ORIGINAL ARTICLE

An evaluation of patients who present to the emergency department with dizziness

Oya Akpınar Oruç[1] **Neşe Nur User**[1]

1 Department of Emergency Medicine, Faculty of Medicine, Afyonkarahisar Health Sciences University. Afyonkarahisar / Türkiye

Abstract

This study aimed to analyze the data of patients presenting with dizziness at our hospital's emergency department (ED) by determining the etiology of dizziness and to contribute to the medical data of our country and the literature. This prospective study was conducted with 116 volunteering patients who presented to the Emergency Department of Afyon Kocatepe University, Faculty of Medicine for one year with dizziness complaints. After the anamnesis, physical examination, diagnostic tests (blood tests, Dix-Hallpike maneuver, audiological-vestibular tests, carotid-vertebral artery color Doppler ultrasonography, and computerized brain tomography), and psychiatric interrogation, the patients were divided into four etiology groups: Peripheral, central, psychogenic, and other causes of dizziness. Clinical features were compared between peripheral and central dizziness groups. A total of 116 (3.4%) of patient admissions to the emergency department complained of dizziness. Forty-nine (42.2%) of these patients were male, 67 (57.8%) were female. In the cohort, 33.9% were under 40, and dizziness increased with older age. Seventy (60.3%) patients had no formal education or were primary school graduates. The initial evaluation at the ED revealed that dizziness mostly shifted with the position (71.6%) and was mainly accompanied by headache (67.2%). Based on their diagnosis, 50 patients (43.1%) were in the peripheral group, 30 patients (25.8%) were in the central group, 22 patients (19%) were in the psychogenic dizziness group, and 14 patients (12%) were in the other causes group. Intergroup analysis between peripheral and central vertigo groups identified that the hearing loss, ear fullness, recent upper respiratory tract infection (URTI), nausea, vomiting, and shifting position was statistically significant ($p<0.05$). Dizziness is one of the common complaints of admission to the ED and may arise from different etiologies. Our study demonstrated that psychogenic dizziness was common in this patient cohort.

Keywords: Dizziness, etiology, emergency department, psychogenic dizziness

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Corresponding Author:
Oya Akpınar Oruç
Email: droyaoruc@gmail.com

Introduction

Dizziness is defined as "a sense of disorientation in space". The symptoms of dizziness described by the patients may occur due to different pathophysiologic situations such as vertigo, ataxia, syncope, and panic attacks. In addition to peripheral and central vestibular system pathologies, many different metabolic, cardiac, and psychiatric causes should be considered in its etiology. In a study conducted by Skiendzielewski et al., on 106 patients with complaints of dizziness, 46 different diseases were identified concerning the etiology [1]. Dizziness affects approximately 20-30% of the general population, is common in general medical practices, and accounts for approximately 2% of emergency admissions [2,3].

Patients who experience dizziness due to peripheral vestibular causes such as benign paroxysmal positional vertigo (BPPV) and vestibular neuritis in the ED may have a benign and self-limiting clinical course. However, dizziness experienced due to central causes such as cerebellar stroke and multiple sclerosis may have more severe consequences. Most admissions to the ED consist of patients with a benign course. Studies have found that 5% of patients presenting to the ED with dizziness have serious neurological diagnoses [4]. It is also possible to detect metabolic, cardiac, and psychogenic causes in the etiology of dizziness in patients without any impairment in vestibular system functions. Various studies have reported that psychogenic factors are responsible for 20-50% of the etiology of dizziness [5]. In today's world, where the number of admissions to the emergency is increasing, it is crucial to understand the etiology in patients with dizziness since it can cause life-threatening conditions in some instances. The etiology of the pathology should be clarified through anamnesis, physical examination, laboratory, and radiological evaluations, and the appropriate treatment should be planned by reviewing the possible causes.

Few studies in our country visited the demographic and clinical characteristics of patients presenting to the ED with dizziness. The present study aimed to determine the demographic and clinical characteristics of this patient cohort, identify the etiological subgroups by making differential diagnoses of dizziness, and contribute to the data collection in the literature and our country.

Materials and Methods

The present prospective study was conducted with 116 patients that presented to the ED with dizziness. The study was carried out with the approval obtained from the Afyon Kocatepe University, Faculty of Medicine Ethics Committee (Registration Number: 2009/7) and the consent of all participants.

The study sample consisted of patients over 18 years of age, who were admitted to the emergency with the complaint of dizziness within a year, and who voluntarily accepted to participate in the study. On the other hand, patients under 18 years of age, those who rejected to participate in the study, patients whose main complaint was not dizziness, and those who were noncompliant with the necessary tests during their follow-up were excluded from the research.

Initially, the vital signs of the patients were evaluated. Next, their demographic data with a detailed anamnesis including the features of their dizziness complaint and the other symptoms accompanying their dizziness were collected, and the physical examination data were recorded for all patients. In addition, a psychiatric interrogation was performed for each patient. Possible clues regarding the etiology of dizziness were sought in patients who underwent general physical and neurological examinations. Subsequently, basic blood tests indicative of body functions was requested.

Cerebral computed tomography imaging (CCT) and carotid-vertebral artery color Doppler ultrasonography (CDUS) were scheduled for the patient group whose etiology was thought to be due to the central pathologies following their initial evaluation in the emergency hall, and possible diagnoses were reviewed. Abnormal findings seen on CCT that were compatible with the patient's clinical status were recorded. In vertebral artery CDUS, cases with a total blood flow of both vertebral arteries below 200 ml/min were considered vertebrobasilar insufficiency. The patient group was also evaluated for any

metabolic and cardiac etiologies of dizziness.

The Dix-Hallpike maneuver was performed in the ED for patients whose etiology was attributed to peripheral pathologies based on the anamnesis and examination findings. The patients were referred to the otorhinolaryngology department for audiological and vestibular tests later under elective conditions. Patients with documented hearing loss were further evaluated for the possible cause of hearing loss and its relationship with dizziness.

In patients with unexplained vestibular dysfunctional etiology and without any metabolic and cardiac causes, antecedent or coexisting psychiatric symptoms with dizziness were interrogated regarding the possibility of psychogenic dizziness [6].

According to their initial evaluation, laboratory, and radiological results, the patients were divided into peripheral, central, psychogenic, and other causes (endocrine, metabolic, cardiac, medication use, and unknown causes) subgroups. Clinical features were compared between peripheral and central dizziness subgroups.

SPSS (Statistical Package for Social Sciences) for Windows 15.0 software was used to analyze the obtained data. Descriptive statistical methods (frequency tables) were used to evaluate the study data. Chi-square test was applied to assess the difference between groups. $p<0.05$ was considered significant.

Results

The present study was conducted in the Emergency Department of Afyon Kocatepe University (AKU), Medical Faculty Hospital, with patients admitted due to dizziness complaints within a year. Of the 15559 patients, 542 (3.4%) presented owing to dizziness. Among these patients, 116 consented to participate in the present study.

Forty-nine (42.2%) patients were male, and 67 (57.8%) were female. The present study observed that admission to the emergency department with dizziness was reported mainly for patients aged 40 years and younger (33.9%) (Table 1).

A review of the patient history data showed that 21 (18.1%) patients had hypertension (HT), four had (3.4%) diabetes mellitus (DM), and seven patients (6%) had both HT and DM. While previous stroke was detected in five patients (4.3%), other health problems were detected in 30 patients (25.9%). Forty-nine patients (42.2%) did not report any comorbid disease (Table 1).

The educational status distribution of the patients showed that 20 patients (17.2%) did not receive any formal education, 50 patients (43.1%) were primary school graduates, 13 patients (11.2%) were secondary school graduates, 18 patients (15.5%) were high school graduates, and 15 patients (12.9%) were university graduates. Thirty-four patients (29.3%) were employed, 76 (65.5%) were unemployed, and six (5.2%) were students.

In terms of dizziness-related symptoms, dizziness shifted with the position (dizziness occurred with positional change) in 83 patients (71.6%), dizziness was accompanied by headache in 78 patients (67.2%), 75 patients (64.7%) had nausea and vomiting with dizziness, and 65 of them (56%) described loss of balance with dizziness. Tinnitus was present in 41 patients (35.3%). Ear fullness with dizziness was reported in 39 patients (33.6%), hearing loss was reported in 32 patients (27.6%), and a recent URTI was found in 21 (18.1%) patients. In addition, dizziness was accompanied by loss of consciousness in 10 (8.6%) patients, visual impairment was observed in seven patients (6%), sensory-motor deficits were observed in six patients (5.2%), and speech impairment was associated with dizziness in three patients (2.6%) (Table 1).

As a result of the history, examination, and diagnostic tests, 50 patients (43.1%) were diagnosed with dizziness from peripheral vestibular system pathologies. Of these patient complaints, 29 (25%) were related to benign paroxysmal positional vertigo, eight were associated (6.9%) with vestibular neuritis, and 13 (11.2%) with other pathologies. Dizziness originating from the central system was identified in 30 patients (25.8%); 13 (11.2%) of these patients were found to be compatible with stroke, 12 (10.3%) with vertebrobasilar system failure, and five (4.3%) with other less

common diagnoses causing centrally induced vertigo. Furthermore, psychogenic dizziness was detected in 22 patients (19%), whereas the presence of dizziness due to other causes (endocrine, metabolic, cardiac, medication use, and unknown causes) was found in 14 patients (12%) (Table 2).

Statistical analysis of disease-related symptoms and signs between peripheral and central vertigo groups showed significant differences in hearing loss, ear fullness, recent infection, nausea, vomiting, and shifting with position (p<0.05). These findings indicate that peripheral vertigo patients have more severe hearing loss, ear fullness, recent URTI, and nausea-vomiting than central vertigo patients. Moreover, it seems that the disease is highly position-dependent in patients with peripheral vertigo. There was no statistically significant difference between the groups in terms of the symptoms of loss of balance, headache, tinnitus, and visual impairment (p>0.05) (Table 3).

Table 1. Distribution of patients according to demographic data.

		Number (*n*)	Percent (%)
Gender	Male	49	42.2
	Female	67	57.8
Age	40≤	39	33.9
	41-50	21	18.3
	51-60	25	21.7
	61≥	30	26.1
History of comorbid diseases	HT	21	18.1
	DM+HT	7	6.0
	Stroke	5	4.3
	DM	4	3.4
	Other	30	25.9
	None	49	42.2
Educational status	Noformal education	20	17.2
	Primary school	50	43.1
	Secondary school	13	11.2
	High school	18	15.5
	University	15	12.9
Work Status	Employed	34	29.3
	Unemployed	76	65.5
	Student	6	5.2
Accompanying symptoms	Shifting with position	83	71.6
	Headache	78	67.2
	Nausea and Vomiting	75	64.7
	Loss of Balance	65	56.0
	Tinnitus	41	35.3
	Ear fullness	39	33.6
	Hearing loss	32	27.6
	Past URTI	21	18.1
	Loss of consciousness	10	8.6
	Speech impairment	3	2.6
	Motor sensory deficit	6	5.2
	Visual impairment	7	6.0

*** HT:** Hypertension; **DM:** Diabetes mellitus

Discussion

The present study aimed to demonstrate the demographic and clinical characteristics of patients admitted to the ED with the complaint of dizziness and to outline their etiology by evaluating their differential diagnosis.

Dizziness is among the most common causes of admission to the ED [7]. A study by Ljunggren et al., reported that approximately 2% of all patients admitted to the ED complained about dizziness yearly [3]. Another study by Newman-Toker et al., stated this frequency as 3.3% [8]. The present study results showed that 3.4% of the patients admitted to the ED within one year presented with dizziness. This finding, supported by previous evidence in the literature, proved that dizziness is one of the most common causes of admissions to the ED of our hospital.

Table 2. Distribution of etiologies of the dizziness.

	Number (*n*)	Percent (%)
Peripheral	50	43.1
BPPV	29	25.0
Vestibular Neuritis	8	6.9
Other	13	11.2
Central	30	25.8
Stroke	13	11.2
Vertebrobasilar Insufficiency	12	10.3
Other	5	4.3
Psychogenic	22	19.0
Other *(Endocrine, metabolic, cardiac, medication use, unknown cause)*	14	12.0

* **BPPV:** Benign Paroxysmal Positional Vertigo

Female patients comprised 57.8% of our study group. A prospective study by Gülalp et al., reported this ratio as 64.6% [9], whereas Navi et al.,'s study reported it as 58% [4]. Although different studies investigating the high incidence of dizziness in women indicated that hormonal changes associated with the premenstrual period or medication use may increase the risk of vestibular system-related diseases, this relationship has not been supported by other studies [10,11]. Nevertheless, the relationship between migraine, which is known to be more common in women, and dizziness may cause the complaint of dizziness to be encountered at a higher rate in women than in men [12].

It was observed that 33.9% of the patients in the present study were younger than 40 years, and the incidence of dizziness increased with age. Other studies in the literature report that dizziness increases with advanced age [13]. It is a fact that vascular risk factors and systemic diseases are more frequently encountered in older ages; thus, the risk of dizziness is increased. Therefore, the result of our study is in concordance with the literature.

Table 3. Distribution of symptoms and *p* values for the peripheral and central vertigo groups.

	Peripheral Vertigo (*n*=50)	Central Vertigo (*n*=30)	*p*
	Number (*n*)	Number (*n*)	
Shifting with position	44	20	**0.037**
Nausea-vomiting	42	18	**0.027**
Loss of balance	35	18	0.366
Headache	33	21	0.716
Tinnitus	23	8	0.080
Hearing loss	22	5	**0.007**
Ear fullness	20	5	**0.020**
Past URTI	17	3	**0.008**
Visual impairment	3	2	0.907
Motor sensory deficit	3	3	0.517
Loss of consciousness	1	5	**0.050**
Speech impairment	1	2	0.293

The present study observed HT in 24.1% of the patients, DM in 9.4%, and previous stroke in 4.3% as comorbid diseases. The study by Warninghoff et al., with 131 patients reported HT in 29% and DM in 6.1% as comorbid diseases in dizzy patients [14]. Various studies have investigated the relationship between dizziness and chronic diseases. For instance, Kao et al., demonstrated the relationship between dizziness and DM [15]. However, although the study by Chang et al., showed a strong relationship between dizziness and stroke, they could not find an exact relationship between dizziness and HT [16]. A different study suggested that dizziness in HT patients may be primarily related to the use of antihypertensive medications [17].

Our study concluded that 68.9% of the patients had dizziness originating from the peripheral and central vestibular systems. Psychogenic causes were identified in 19% of the patients, and other causes such as endocrine, metabolic, and cardiac problems, medication use, and unknown causes seemed in the etiology in 12% of the patients. It has been observed that dizziness originating from the vestibular system is mainly related to peripheral causes (43.1%), while central-related causes occur less frequently (25.8%). There are differences between the results from various studies using different methodologies for evaluating patients presenting to the ED with dizziness. In a review by Kroenke et al., the etiology was peripheral vestibular causes in 44%, psychogenic causes in 16%, central vestibular causes in 11%, other causes in 26%, and the underlying condition remained obscure in 13% of patients [18]. In the study conducted by Newman-Toker et al., with 9472 dizziness patients admitted to the ED, peripheral vestibular causes were observed in 32.9%, central in 11.2%, and psychogenic in 7.2% of the patients [8].

On the other hand, Koçer et al., found 41.3% peripheral, 4.9% central, 13.1% systemic, and 0.3% psychiatric causes in the etiology of dizziness patients who presented to the ED [19]. It can be concluded that the results obtained in the etiologic evaluation of dizzy patients differ.

The difference in results may be due to the

diversity of methodologies used in the studies or demographic parameters in the patient groups.

The high rate of psychogenic causes in the etiology of dizziness is one of the most striking results of the present study. The frequency of psychogenic dizziness in this patient cohort has been previously reported at varying rates. Newman-Toker et al., found this rate as 7.2%, but Kroenkebet al.,'s study reported dizziness associated with psychiatric diseases in 40% of the patients [8,20]. Psychogenic dizziness may occur without vestibular dysfunction as a symptom in anxiety, depression, conversion, posttraumatic stress disorder, and rarely in psychosis [6,21]. The fact that dizziness can be explained neither by vestibular dysfunction nor by metabolic or cardiac causes and the presence of antecedent or coexisting psychiatric symptoms accompanying vertigo supports the diagnosis of psychogenic dizziness. In the study by Chang et al., it was found that people who experience severe stress and depression experience more dizziness [16]. Gomez et al.,'s study stated that poor socioeconomic conditions such as insufficient income, low education level, low social status, and unemployment might trigger dizziness at a higher rate as a source of psychological stress [22]. In the present study, most of the patients had low income, and their education levels might have facilitated the development of psychogenic dizziness.

Although low mortality is reported in dizzy patients, reasons such as delayed or incomplete evaluation of the pathology and loss of time in cases that require urgent intervention, which is imperative in patients with vertigo originating from the central vestibular system, may cause an increase in morbidity and mortality. It should be remembered that vascular occlusions of the posterior fossa can mimic peripheral vestibular diseases. However, in a study by Idil et al., it was reported that the incidence of a central neurological pathology in patients with isolated dizziness is scarce [23]. Shahrami et al., proved that anamnesis and clinical examination have high sensitivity and specificity in differentiating peripheral and central vertigo [24]. Their study reported that nausea, vomiting, and headache are more common in peripheral vestibular system-induced dizziness in patients. In the present study, the dizziness shifting with position, the presence of nausea-vomiting, hearing loss, and ear fullness, a history of previous URTI, and the frequency of loss of consciousness showed a significant difference between vertigo patient groups originating from the peripheral and central vestibular system, which is parallel to the evidence in literature [25,26]. In most cases, it will be possible to avoid unnecessary tests and waste time in patients evaluated for dizziness only with a detailed anamnesis and physical/ neurological examination.

The limitations of the present study include the small number of patients, the difficulty of access to detailed radiologic interventions such as Magnetic Resonance Imaging, which may lead to a straighter forward diagnosis in the ED, the methodological differences between the etiological classifications in previous studies, and the difficulties in interpreting our study in the light of these.

Conclusion

In this study, data on dizzy patients who came to the emergency department of our hospital were presented. Dizziness is one of the frequent causes of admission to the emergency department, and many different diseases can be detected in the etiology. The high rate of psychogenic dizziness in the etiology is one of the remarkable results of this study. In the differential diagnosis of patients evaluated in the emergency department due to dizziness, the diagnosis of psychogenic dizziness should be kept in mind. With the right diagnosis and correct treatment planning, it will be possible to increase the quality of life and prevent loss of time and labor.

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Conflict of interest

The authors approve that there is no conflict of interest.

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ORIGINAL ARTICLE

Comparison of two different surgical techniques in the treatment of Fournier's Gangrene

Hasan Anıl Kurt[1] **Emre Onur Güven**[1]

1 Department of Urology, Medical Faculty, Çanakkale Onsekiz Mart University. Çanakkale / Türkiye

Abstract

Fournier's gangrene is a rapidly progressive, fatal, necrotizing fasciitis of the perineum and penoscrotal region which requires rapid intervention. This retrospective study compares the surgical outcomes of the fasciocutaneous flap and the embedding of the testicles into the thigh skin, applied for the reconstruction of penoscrotal defects after surgical debridement due to Fournier's gangrene, in the light of the literature. A total of 110 patients treated for Fournier's gangrene at Çanakkale Onsekiz Mart University, Faculty of Medicine, Department of Urology, Urology Clinic between 2009 and 2021 were evaluated retrospectively. Among these, 82 patients treated with fasciocutaneous flap and embedding of the testicles into the thigh skin for the reconstruction of penoscrotal defects were included in the study. For these two wound closure methods, the cases were compared in age, hospital stay after debridement, hospital stay after wound closure, size of the debrided area, and postoperative complication parameters. There was no significant difference between the two groups in terms of age, comorbidity (hypertension, diabetes mellitus, etc.), and hospital stay after debridement. However, the length of hospital stay after wound closure and the size of the debrided area were significantly higher in patients with fasciocutaneous flap compared to the method in which the testis was embedded in the thigh. The fasciocutaneous flap application, which we apply for defects larger than 50% of the scrotum or extending beyond the scrotum, is a method that can be preferred by experienced surgeons for wound closure after Fournier gangrene debridement, considering patient comfort, since it does not create tension and blood supply to the testis is more comfortable. However, it would be more appropriate for the clinician to make a profit-loss calculation due to both the length of the operation and its more complex nature and the prolongation of the hospital stay after wound closure.

Keywords: Fournier's gangrene, debridement, fasciocutaneous flap

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Corresponding Author:
Hasan Anıl Kurt
Email: doktoranil@yahoo.com

Introduction

Although Fournier's gangrene (FG) was first coined by Jean Alfred Fournier in 1883 as a syndrome with perineal necrosis in males, it was first described by Baurienne in 1764 [1]. Wilson was the first scientist to describe necrosis of the fascia as necrotizing fasciitis [2]. Fournier's gangrene is a rapidly progressive, fatal, necrotizing fasciitis of the perineum and penoscrotal region (which may also involve the rectum) (Fig. 1) [3].

Figure 1. Fournier's gangrene before operation.

FG has incidence rate of approximately 1.6 per 100,000 males [4]. Joseph Jones, a military surgeon, first described the mortality rate of 2642 soldiers affected by FG in the civil war as 46% in 1871 [5]. In 2000, Eke compiled 1726 cases and reported a mortality rate of 16% [6]. Indeed, some studies have reported case fatality ratios reaching 66% [7,8].

Understanding how FG spreads from the deep fascia of the urogenital and anogenital region to the abdomen and chest requires a look at its anatomy. Although the infection originates from the skin, urethra or rectum, the formation of thrombosis in the small subcutaneous vessels in the later stages and the anaerobic factors also contribute to infection [9,10]. This initially painful condition turns into a locally hypoesthetic and even anesthetic condition with the infarction of nerve cells [11]. This infectious state may progress and cause soft tissue destruction and sepsis at a rate of 2-3 cm/hour [12]. The initial protection of the superficial layers and skin from infection, and the spread of necrosis along the fascial planes, may cause the disease to be underestimated by inspection and lead to delayed diagnosis. The spermatic fascia and vascular network, which are independent of the vascular supply of the urogenital region and come from the retroperitoneum, often protect the testicles from infectious involvement. Likewise, the deep Buck's fascia surrounding the urethra and corpora cavernosa prevents the spread of FG.

In majority of the cases, conditions that impair the resistance of the general body and immune system or comorbidities that facilitate infection can be detected in the history and during clinical follow-up [3]. Yet, the underlying cause could not be determined in 20% of the cases.

Although the cases are polymicrobial, the most common microorganism is *Escherichia coli.* (48%) Following this, Morua et al. reported that *Enterococcus faecalis* was involved in 28% of the cases [13]. Staphylococcus and Pseudomonas predominate in most of the remaining cases. Treatment requires cleaning of the necrotic tissue with aggressive surgical intervention. Antibiotherapy, on the other hand, requires broad-spectrum antibiotics with good anaerobic activity, especially against Staphylococcus and Pseudomonas species [14].

FG may give clinical findings similar to milder infections with erythema and cellulitis. The stage of this infection should be evaluated together with the general condition of the patient. However, in case of pain disproportionate to the findings in the examination, necrotizing fasciitis should come to mind [15]. Cellulitis and erysipelas may present with well-defined areas of erythema or inflammation, whereas necrotizing fasciitis is characterized by erythema with limited borders. In the differential diagnosis of FG, many diseases such as polyarteritis nodosa, strangulated hernia, scrotal or ischiorectal abscess, balanitis, pyoderma gangrenosum, warfarin necrosis and ecthyma gangrenosum may come to mind [16].

The foul-smelling "dishwater" pus that may be encountered during surgical debridement is indicative of tissue necrosis and characterizes

necrotizing fasciitis. If FG is not intervened quickly enough, it can cause the infection to spread rapidly and even cause death with developing multi-organ failure. Conducting mortality research in FG, Yan et al. It has been shown that early treatment reduces mortality [17,18]. 1463 cases were analyzed in the review of the cases between 1980-2003 by Goh et al [15]. Pain, redness and swelling were the most common clinical findings seen in more than 70% of cases. Crepitation seen in later stages can be seen as a result of exotoxins of anaerobic infections causing tissue necrosis.

The most specific imaging modality for determining the extent of infection is computed tomography (CT), which allows surgical teams to plan debridement accordingly [19]. When other imaging modalities are insufficient to determine the extent of infection, magnetic resonance imaging (MRI) is used [20]. Although MRI can aid in the diagnosis, its utility is limited due to the rapid progression of FG and should not be used to postpone surgical interventions [20].

Scrotal skin loss after FG debridement can be more than 50%. Many reconstructive techniques have been described for the preservation of testicular functions and a good aesthetic result. The size and direction of the defect are critical for the technique to be used. At this point, most clinicians plan the appropriate surgery based on scrotal skin loss.

The choice of anesthesia technique is also important in FG. General anesthesia is preferred to control physiological homeostasis [21]. Koitabashi et al., recommended avoiding spinal anesthesia in the presence of lumbar subcutaneous gas [22].

After the operation, in addition to the traditional sterile wet dressing, other methods such as hyperbaric oxygen, growth agents, unprocessed honey, and vacuum dressing technology can be applied [23].

This retrospective study compares the surgical outcomes of the fasciocutaneous flap and the embedding of the testicles into the thigh skin, applied for the reconstruction of penoscrotal defects after surgical debridement due to Fournier's gangrene, in the light of the literature.

Materials and Methods

A total of 110 patients treated for Fournier's gangrene at Çanakkale Onsekiz Mart University, Faculty of Medicine, Department of Urology, Urology Clinic between 2009 and 2021 were evaluated retrospectively. Among these, 82 patients treated with fasciocutaneous flap and embedding of the testicles into the thigh skin for the reconstruction of penoscrotal defects were included in the study. For these two wound closure methods, the cases were compared in age, hospital stay after debridement, hospital stay after wound closure, size of the debrided area, and postoperative complication parameters.

Figure 2. Granulation tissue after debridement.

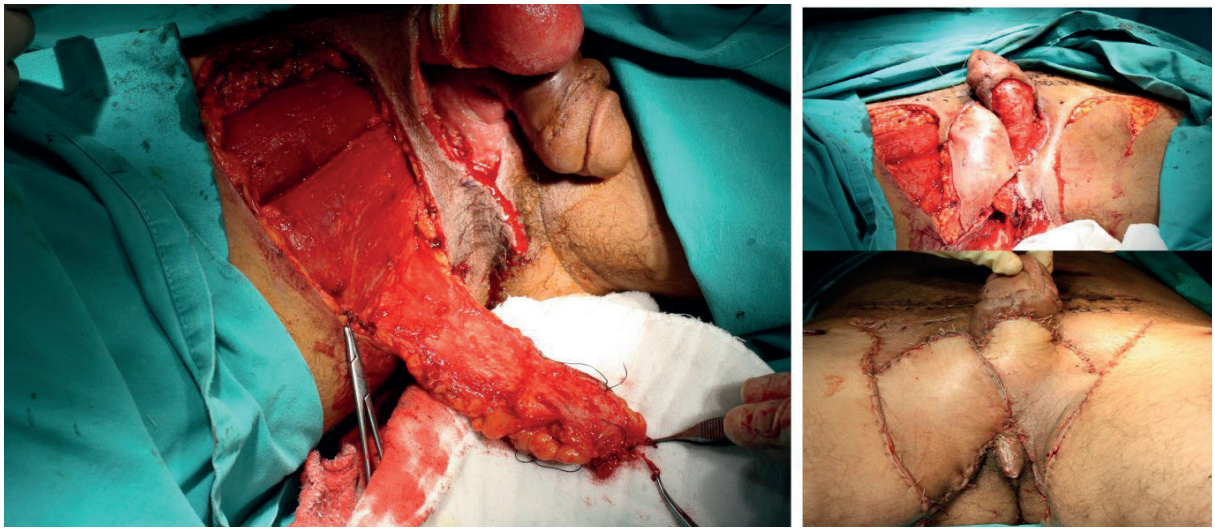

Figure 3. Fasciocutaneous flap method.

Figure 4. Embedding the testicle in the thigh method.

The study was approved by the Social and Humanity Sciences Ethical Committee of Canakkale Onsekiz Mart University Medical Faculty with the number 2011-KAEK-27/2021-E.2100003815.

Surgical Techniques

Fasiocutaneous flap: Following the healing of the patient's wound site, the operation was started together with the urology and plastic surgery clinics by positioning the legs in abduction. The defect edges in the penoscrotal region were debrided. First, the right transverse fasciocutaneous flap was prepared in accordance with the drawing made before, and it was raised on the vascular handle and brought to the right penoscrotal area by turning it over the pedicle to the site that exposed the testis. This flap closed the defect on the right side. Then, the same flap was prepared from the left side in the same way, and the left side defect was completely closed. (Fig. 2,3)

Embedding the testis in the thigh: Following the healing of the wound site, the incision lines in the suprapubic, scrotal, inguinal and perineal regions were debrided by placing a Foley catheter under sterile conditions in the lithotomy position. The membranous portions were excised. Granulation was observed on the tissues. With blunt dissection, pockets were created in the subcutaneous region of both thighs where the testicles could sit comfortably. After placing 2 hemovac drains in the lodge and 1 under the skin and controlling the bleeding, the layers were closed in the anatomical plane, and the operation was completed. (Fig. 4)

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The Chi-square test and Mann-Whitney U-test were used to compare categorical data between groups. Results with a p value of <0.05 were considered significant.

All 82 patients were male. The method chosen for the reconstruction of penoscrotal defects was fasciocutaneous flaps in 15 (18%) patients and embedding the testicles into the thigh in 67 (82%) patients. Of our patients, 40 (48%) had Type 2 Diabetes Mellitus (Type 2 DM), and 27 (67.5%) of these Type 2 DM patients had uncontrolled blood sugar. Vascular disease (hypertension, peripheral artery disease, coronary artery disease) was present in 50 (60%) patients. Comorbidities were similar in both groups. The mean age of the patients with fasciocutaneous flap and with testicle embedding in the thigh were 53 (±9.7)

Table 1. Comparison of fasciocutaneous flap and embedding the testicle in the thigh methods.

	Fasciocutaneous flap	Embedding the testicle in the thigh
Number	15 (18%)	67 (82%)
Age	53 ± 9.7	57 ± 8.2
Duration of hospitalization after debridement	12.1 ± 2.4	12.8 ± 2.3
Duration of hospitalization after wound closure	13.5 ± 2.7	2.4 ± 1.7
Size of debrided area (cm^2)	78 ± 17.9	35 ± 14.1

and 57 (± 8.2), respectively. After debridement, the patients who underwent fasciocutaneous flap surgery stayed in the hospital for 12.1 (±2.4) days, while those who underwent testicle embedding surgery remained in the hospital for 12.8 (±2.3). The groups had no significant difference in age, comorbidity, and length of hospital stay after debridement. However, the length of hospital stay after the reconstruction of penoscrotal defects was significantly longer in patients with fasciocutaneous flap (13.5±2.7) compared to the method in which the testicles were embedded in the thigh skin (2.4±1.7). The size of the debrided area was also significantly larger in patients with a fasciocutaneous flap (78±17.9 cm^2) compared to those with testicle embedding into the thigh skin (35±14.1 cm^2).

Discussion

Fournier's gangrene is a rapidly progressive, fatal, necrotizing fasciitis of the perineum and penoscrotal region (which may also involve the rectum) which requires rapid intervention [3]. Some studies have reported case fatality ratios reaching 66% [7,8]. Although the infection originates from the skin, urethra or rectum, the formation of thrombosis in the small subcutaneous vessels in the later stages and the anaerobic factors also contribute to infection [9,10]. This initially painful condition turns into a locally hypoesthetic and even anesthetic condition with the infarction of nerve cells [11].

Demographics indicate male predominance. Of the 25 million patients in the US State Inpatient Database, only 39 (2%) of 1641 patients operated on for FG were women. In our study, all patients were male.

Conditions that impair the resistance of the general body and immune system or comorbidities that facilitate infection can be detected in the history and during clinical follow-up in most cases [3]. Yet, the underlying cause could not be determined in 20% of the cases. Co-morbidities are present on the basis of FG development in up to 88% of patients [23,24]. The most common of these is diabetes (27-60%) [15,16]. In addition, obesity, hypertension, peripheral vascular disease and alcoholism can be considered as risk factors for FG development. In our study, 40 (48%) of our patients had Type 2 Diabetes Mellitus (Type 2 DM), and 27 (67.5%) of these Type 2 DM patients had uncontrolled blood sugar. Vascular disease (hypertension, peripheral artery disease, coronary artery disease) was present in 50 (60%) patients. Both groups had similar comorbidities.

The use of multiple antibiotics is recommended in the treatment of FG; because FG is a polymicrobial infection involving anaerobes. Appropriate treatment is metronidazole for anaerobes, penicillin for streptococci, and third generation cephalosporins for gram-negatives [26]. Despite prolonging wound healing, wide resection (including the surgical margin with good tissue) is recommended by some surgeons [25]. In order to completely clear the necrosis, it is recommended to finish the debridement at a level where the skin cannot be easily separated from the subcutaneous tissue [27].

Granulation tissue develops after the treatment of Fournier's gangrene, indicating that the appropriate time has come for reconstruction surgery. Scrotal skin loss after FG debridement can be more than 50%. Many reconstructive techniques have been described for the preservation of testicular functions and a good aesthetic result. It is important that the surgical method is reconstructive in order to shorten the hospital stay and to support the patient cosmetically and psychologically. The size and direction of the defect are critical for the technique to be used. At this point, most clinicians plan the appropriate surgery based on scrotal skin loss.

When we evaluated grafting techniques such as transposition into a subcutaneous pocket with vascularized pedicles of the testis and spermatic cord, and tissue expansion techniques (such as the pedicled gracilis flap), Horta et al., showed that some kind of reconstructive surgery was needed in 67% of the patients [28,29]. They concluded that a scrotal loss less than 50% could be closed with a primary/scrotal skin flap according to the tension, or the testis could be buried under the skin of the thigh by stretching the scrotal skin [30,31]. However, skin grafting or flap reconstruction has been recommended for defects greater than 50% of the scrotum or

extending beyond the scrotum [32].

Testicular gas (produced by bacteria) detected by imaging methods can almost be associated with orchiectomy [33]. It was observed that the mortality risk decreased by 70% in patients requiring orchiectomy.

Considering the disadvantages of wide excision of necrotic tissue, Watanabe et al., showed successful results in follow-up with multiple subcutaneous Penrose drains in addition to limited excision [34]. Adequate nutritional status or energy intake is also necessary during the treatment process [35].

In this retrospective study, we compared the surgical outcomes of the fasciocutaneous flap and the embedding of the testicles into the thigh skin, applied for the reconstruction of penoscrotal defects after surgical debridement due to Fournier's gangrene in 82 patients at Çanakkale Onsekiz Mart University, Faculty of Medicine, Department of Urology, between 2009-2021, in the light of the literature.

There was no significant difference between the two groups in terms of age, comorbidity hypertension, diabetes mellitus, etc.), and the length of hospital stay after debridement. However, the length of hospital stay after wound closure and the size of the debrided area were significantly higher in patients with a fasciocutaneous flap compared to those with embedding of the testicles into the thigh.

Conclusion

The fasciocutaneous flap application, which we apply for defects larger than 50% of the scrotum or extending beyond the scrotum, is a method that can be preferred by experienced surgeons for wound closure after Fournier gangrene debridement, considering patient comfort, since it does not create tension and blood supply to the testis is more comfortable. However, it would be more appropriate for the clinician to make a profit-loss calculation due to both the length of the operation and its more complex nature and the prolongation of the hospital stay after wound closure.

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Conflict of interest

No potential conflict of interest was reported by the authors.

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