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## **AIRTRAO® VERSUS MACINTOSH LARYNGOSCOPE FOR AIRWAY MANAGEMENT DURING GENERAL ANESTHESIA:** A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Maciej Maslanka<sup>1,2</sup>, Jacek Smereka<sup>2,3</sup>, Michal Pruc<sup>2</sup>, Oliver Robak<sup>4</sup>, Kecskés Attila<sup>5</sup>, Lukasz Szarpak<sup>1,2,6</sup>, Kurt Ruetzler<sup>7</sup>

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#### ABSTRACT

INTRODUCTION: Despite the introduction of supraglottic devices for ventilation, endotracheal intubation is still a gold standard for airway management in both prehospital and operating theatre conditions. This systematic review and meta-analysis were conducted to investigate the effectiveness and safety of Airtrag vs. Macintosh laryngoscope for endotracheal intubation during general anesthesia.

MATERIAL AND METHODS: The current issue of Pubmed, Embase, Cochrane, Web of science, Scopus (from database inception to October 20, 2020) was searched. Randomized controlled trials (RCT) comparing Airtrag and Macintosh laryngoscope were included in this meta-analysis. The primary outcomes were the success rate of first attempt intubation and intubation time. Secondary outcomes were overall intubation success rate, malposition, and adverse events. Review Manager 5.4 software was used to perform the pooled analysis and assess the risk of bias for each eligible RCT.

RESULTS: Seventeen studies were included in the review for data extraction. First attempt success rate was 85.6% for ATQ vs. 68.4% for MAC (OR = 3.00; 95% CI: 1.37, 6.60; p = 0.006;  $I^2 = 63$ %). The use of ATQ and MAC for intubation in cervical spine immobilization was associated with the effectiveness of the first intubation attempt at 98.6% vs. 71.1% (OR = 16.40; 95% CI: 3.55, 78.87; p < 0.001;  $I^2 = 0$ %). Intubation time with ATQ was shorter than with MAC (MD = -3.19; 95% CI: -9.33, 2.95; p = 0.31;  $I^2$  = 97%). The endotracheal intubation during cervical spinal intubation was associated with significantly shorter procedure duration for ATQ than for MAC (MD = -10.30; 95% CI: -18.43, -2.18; p = 0.01; I<sup>2</sup> = 74%). The total efficacy of intubation, which for ATQ and MAC varied and was 86.7% vs. 80.6% respectively (OR = 2.88; 95% CI: 1.61, 5.13; p < 0.001;  $I^2 = 0$ %).

CONCLUSIONS: Based on the results of this analysis, we conclude that ATQ can reduce the failed first intubation attempt, especially in cervical manual inline stabilization patients, and reduces the time needed to obtain airway management, but does not provide significant benefits on other adverse events associated

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with tracheal intubation. Further studies are needed to demonstrate whether severe adverse events are significantly different between the two devices.

KEY WORDS: airway management, endotracheal intubation, laryngoscope, systematic review, meta-analysis Disaster Emerg Med J 2021; 6(1): 1–9

#### **INTRODUCTION**

Various surgical procedures are performed under local and regional anesthesia. Much of the surgical procedures can be performed using supraglottic devices, but still, in many surgical procedures, general anesthesia is performed with airway protection by endotracheal intubation [1].

Providing adequate patient ventilation, airway management and especially endotracheal intubation are the basic procedures performed by an anesthesiologist [2]. Unfortunately, in some cases, endotracheal intubation is more or less difficult and in some cases may not be possible [3, 4]. There are several scales for assessing the patient's airway and possible difficulties in endotracheal intubation. These scales facilitate the selection of the right technique, the preparation of appropriate equipment, including alternative ones, and above all, is based on the involvement of experienced medical personnel.

Improper airway management may result in a variety of complications, including the risk of death. This is particularly important in emergency and life-saving patients and airway procedures in emergency medicine. Unrecognized esophageal intubation may have catastrophic consequences for the patient [3]. The problem of difficult airways is particularly important in patients with the severe clinical course of COVID-19, where hypoxia progresses very quickly and difficulties in securing the airway may pose a real threat to the patient's life, especially in case of limitations for medical personnel related to the use of personal protective equipment and lack of instant assistance from more experienced medical personnel [5].

Various parameters can be used to assess the efficacy of airway management especially endotracheal intubation, including the total duration of the procedure, the percentage of successful intubations at the first attempt, the total number of intubation attempts, and the complications of endotracheal intubation for both normal and difficult airways, including cervical spine immobilization.

This systematic review and meta-analysis was conducted to investigate the effectiveness and safety of Airtraq vs. Macintosh laryngoscope for endotracheal intubation during general anesthesia.

#### MATERIAL AND METHODS

This systematic review and meta-analysis was conducted following the recommendations of The Cochrane Handbook for Systematic Reviews of Interventions and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [6]. Before starting the study, all authors agreed on the analysis methods and the inclusion and exclusion criteria to be applied.

#### Data sources and search strategy

Two authors (M.M. and L.S.) independently searched relevant literature. The current issue of Pubmed, Embase, Cochrane, Web of science, Scopus (from database inception to October 20, 2020) was searched. Study authors were mailed for any useful information. The whole search strategy used free words including 'Airtraq' OR 'ATQ' OR 'channeled laryngoscop\*' AND 'Macintosh' OR 'MAC' OR 'direct laryngoscop\*' AND 'endotracheal intubation' OR 'tracheal intubation' OR 'intubation' OR 'airway' OR 'airway management' OR 'ETI'. The reference lists of all eligible trials and reviews were screened for additional citations. We restricted publication to the English language.

#### **Eligibility criteria**

Randomized controlled trials comparing Airtraq and Macintosh laryngoscope and reporting the efficacy parameters of tracheal intubations were included. The pre-hospital study, conference papers, letters to the editor, cadaver study, simulated study, or case reports were excluded.

#### **Data extraction**

Two reviewers (M.M. and J.S.) independently extracted data from each study by using a predefined data extraction form. Any disagreement unresolved by the discussion was resolved in consultation with a third reviewer (L.S.). The following variables were extracted from the studies: first author name, country, study design, airway management setting, type of operator, no. of patients, age, sex, the success of intubation attempts, intubation time, adverse events, inclusion and exclusion criteria, outcomes and findings. In case if the above variables were not found in the articles, we requested the data from their authors via email.

#### **Risk of bias assessment**

The risk of bias for each eligible study was independently assessed by two review authors (J.S. and M.M.). For randomized controlled trials, the Cochrane Collaboration's tool (The Cochrane Collaboration, Oxford, UK) was used to assess the risk of bias [7]. This tool is widely used to assess the methodological quality of RCTs and consists of the following six items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting. According to the previous trials [8] each bias was graded 'yes', 'no', or 'unclear', which reflected a high risk of bias, low risk of bias, and uncertain bias, respectively.

#### **Statistical analysis**

Meta-analysis was performed by RevMan 5.4EN (Cochrane Collaboration, Oxford, UK). A two-tailed p < 0.05 was considered statistically significant. All statistical variables were determined with 95% confidence interval (CI) to estimate the range of plausible treatment effects. In case when the continuous outcome was reported in a study as median, range, and interquartile range, we estimated means and standard deviations using the formula described by Hozo et al. [9]. We employed the inverse-variance method for the continuous outcomes and the Mantel-Haenszel models for all dichotomous outcomes. We calculated mean differences (MD) for continuous measurements and odds ratios (OR) for dichotomous outcomes.

Statistical heterogeneity across trials was estimated using the I<sup>2</sup> statistic [10], in which I<sup>2</sup> < 30% denotes 'low heterogeneity', I<sup>2</sup> = 30% to 50% represents 'moderate heterogeneity', and I<sup>2</sup> > 50% denotes 'substantial heterogeneity' [11]. The random-effects model was used for I<sup>2</sup> > 50%; otherwise, the fixed effects model was employed. The Mantel-Haenszel method was used to synthesize dichotomous data.

#### RESULTS

#### Characteristics of included studies

The search strategy details are provided in Figure 1. Using a search strategy, a total of 507 papers were identified. A total of 136 studies were removed due to duplicates. In the remaining 371 studies, 329 were excluded because of patients not eligible for the study purpose, abstract unavailable, reviews, or letters.

Twenty-five articles were excluded as follows: four were not RCT designed studies, four were only published abstracts, three were letters to the editor, seven evaluated different outcomes to this study (for the transitivity assumption not to be violated), six were simulation trials, and one was a redundant publication. Finally, 17 studies were eventually included in the review for data extraction [12–28].

#### **Risk of bias assessment for included studies**

Detailed description regarding the risk of bias of the included studies is shown in Supplementary digital content (SDC) of the 17 included studies, all were RCTs [12–28], and six of them were single-blinded [12, 13, 22–25]. All studies (100%) were assessed as having a low risk of bias about selective reporting and other potential sources of bias.

#### **Primary outcome**

Twelve studies (n = 782 patients) reported the first attempt success rate of intubation with ATQ and MAC [12, 13, 17, 18, 20–26, 28]. In case of ATQ first attempt success rate was 85.6% vs. 68.4% for MAC (OR = 3.00; 95% Cl: 1.37, 6.60; p = 0.006;  $I^2 = 63\%$ ; Figure 2). The additional analysis showed that the use of ATQ and MAC in cervical spine immobilization was associated with the effectiveness of the first intubation attempt at 98.6% vs. 71.1% (OR = 16.40; 95% Cl: 3.55, 78.87; p < 0.001;  $I^2 = 0\%$ ) respectively.

The intubation time was reported in fourteen publications with ATQ was shorter than with MAC (MD = -3.19; 95% Cl: -9.33, 2.95; p = 0.31;  $I^2 = 97\%$ ; Figure 3) [12, 13, 15–17, 19, 21–28]. The endotracheal intubation during cervical spinal intubation was associated with significantly shorter procedure duration for ATQ than for MAC (MD = -10.30; 95% Cl: -18.43, -2.18; p = 0.01;  $I^2 = 74\%$ ). For intubation without cervical immobilization of the spine a slight superiority of ATQ over MAC in terms of intubation time was noted (MD = -82; 95% Cl: -7.85, 6.20; p = 0.82;  $I^2 = 98\%$ ).

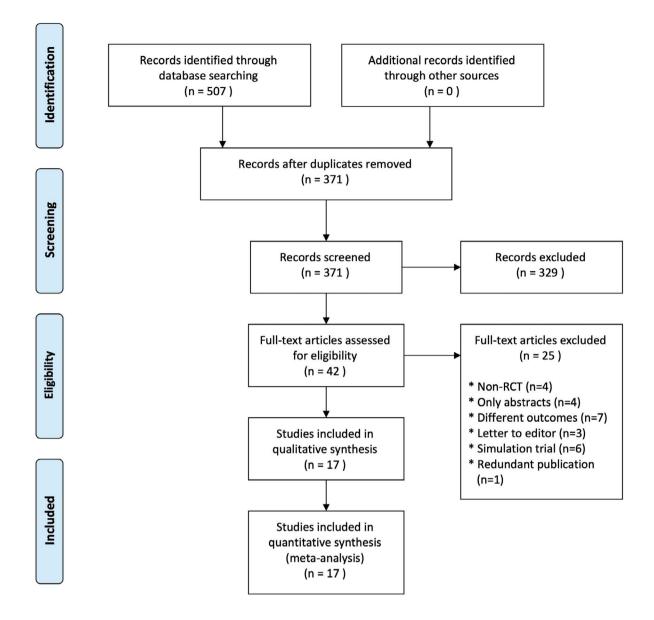


FIGURE 1. Flow diagram showing stages of database searching and study selection

	ATC	2	MAG	2		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
Abdallah 2019	34	35	33	35	6.2%	2.06 [0.18, 23.83]	
Al-Ghamdi 2016	9	21	16	22	11.1%	0.28 [0.08, 1.01]	
Ertürk 2015	30	40	20	40	12.8%	3.00 [1.16, 7.73]	
Ferrando 2011	29	30	24	30	7.1%	7.25 [0.82, 64.46]	
Hosalli 2017	27	30	23	30	10.2%	2.74 [0.63, 11.82]	
Koh 2010	24	25	10	25	7.2%	36.00 [4.17, 310.44]	<b>→</b>
Maharaj 2006	30	30	29	30	4.3%	3.10 [0.12, 79.23]	
Maharaj 2007	20	20	19	20	4.3%	3.15 [0.12, 82.16]	
Maharaj 2008	19	20	13	20	7.0%	10.23 [1.12, 93.34]	
McElwain 2011	28	28	25	31	5.0%	14.53 [0.78, 270.92]	
Nishiyama 2011	29	36	31	35	10.8%	0.53 [0.14, 2.02]	
Zhao 2014	54	74	26	75	14.0%	5.09 [2.53, 10.24]	
Total (95% CI)		389		393	100.0%	3.00 [1.37, 6.60]	-
Total events	333		269				
Heterogeneity: Tau <sup>2</sup> =	= 1.03; Cl	$ni^2 = 30$	0.04, df =	= 11 (P	= 0.002)	$; I^2 = 63\%$	0.01 0.1 1 10 100
Test for overall effect	: Z = 2.73	3 (P = 0)	0.006)				0.01 0.1 1 10 100 Favours [ATQ] Favours [MAC]

FIGURE 2. Forest plot of first intubation attempt success rate in Airtraq vs. Macintosh groups. The center of each square represents the odds ratio for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

		ATQ		j	MAC			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Abdallah 2019	11.5	4.36	35	14.18	3.42	35	7.8%	-2.68 [-4.52, -0.84]	-
Al-Ghamdi 2016	56.4	6.02	21	35.1	8.61	22	7.5%	21.30 [16.88, 25.72]	
Chalkeidis 2010	29.6	8.5	35	23.7	5.9	28	7.6%	5.90 [2.34, 9.46]	
Ertürk 2015	31.5	20.8	40	24.3	15.3	40	6.9%	7.20 [-0.80, 15.20]	
Hindman 2014	19.6	7	14	21.6	7.8	14	7.3%	-2.00 [-7.49, 3.49]	
Koh 2010	49.8	33.6	25	90	49.4	25	3.7%	-40.20 [-63.62, -16.78]	←
Maharaj 2006	12.2	8.5	30	12.4	9.2	30	7.5%	-0.20 [-4.68, 4.28]	
Maharaj 2007	13.2	5.4	20	20.3	12.2	20	7.3%	-7.10 [-12.95, -1.25]	
Maharaj 2008	13.4	6.3	20	47.7	8.5	20	7.5%	-34.30 [-38.94, -29.66]	
McElwain 2011	19.8	3.8	29	26.8	9.5	31	7.6%	-7.00 [-10.62, -3.38]	
Nishiyama 2011	39.8	14.2	36	36.5	18.5	35	7.0%	3.30 [-4.39, 10.99]	
Vijayakumar 2016	25.8	3.8	45	22.4	2.8	45	7.8%	3.40 [2.02, 4.78]	~
Zhao 2014	68	21	74	96	22	75	7.1%	-28.00 [-34.91, -21.09]	
Çolak 2015	29.8	13.82	46	13.59	5.49	49	7.5%	16.21 [11.93, 20.49]	
Total (95% CI)			470			469	100.0%	-3.19 [-9.33, 2.95]	•
Heterogeneity: Tau <sup>2</sup> =	= 125.72	• Chi <sup>2</sup> =	= 494 4	16 df =	13 (P	< 0.00	$(001) \cdot 1^2 =$		
Test for overall effect				, ui –	(1		,, -		-50 -25 0 25 50 Favours [ATQ] Favours [MAC]

FIGURE 3. Forest plot of intubation time rate in Airtraq vs. Macintosh groups. The center of each square represents the mean difference for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

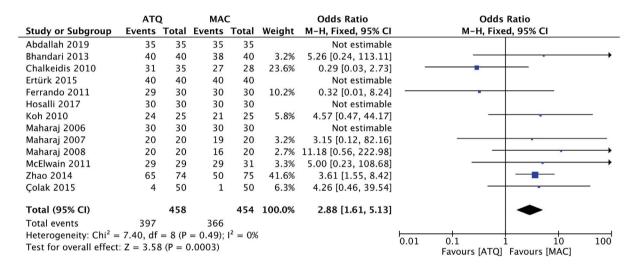


FIGURE 4. Forest plot of the overall intubation success rate in Airtraq vs. Macintosh groups. The center of each square represents the odds ratio for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

#### Secondary outcomes

Thirteen studies indicated the total effectiveness of intubation, which for ATQ and MAC varied 86.7% vs. 80.6% respectively (OR = 2.88; 95% Cl: 1.61, 5.13; p < 0.001;  $I^2 = 0\%$ ; Figure 4) [12, 14–18, 20–25, 28].

One study [16] indicated that cervical spine movements were lower for ATQ intubation than for MAC (MD = -12.70; 0.5% CI: -14.92, -10.48; p < 0.001).

Pooled analysis showed that ATQ intubation required less head positioning change during the procedure (23.0%) than MAC (32.1%; OR = 0.23; 95% Cl: 0.01, 5.16; p = 0.35; l<sup>2</sup> = 87%). The need for external laryngeal manipulation was also lower (3.3%) with ATQ than with MAC (36.6%; OR = 0.07; 95% Cl: 0.04, 0.13; p < 0.001; l<sup>2</sup> = 28%).

#### Adverse events

A detailed list of adverse events is presented in Table 2. The most common complication among the studies included in the meta-analysis was a sore throat and it concerned 41.7% of patients intubated with ATQ and 57.7% of those intubated with MAC. Intubation with ATQ was associated with a lower risk of blood staining of laryngoscope blade, laryngospasm, and mucosal trauma compared to MAC. In the case of lips trauma, an inverse relationship was noted, where trauma with ATQ was more than 5.5% higher than with MAC.

#### DISCUSSION

In this review, we showed that Airtraq was the most useful device in terms of the success rate of the first

Table 1. Characteristics of included studies	cs of inclue	ded studies										
Study	Country	Study design	Intubation setting	Operator	No partic	No. of participants	Age	je	Sex, I	Sex, male	Success of first intubation attempt	st intubation npt
					ATQ	MAC	ATQ	MAC	ATQ	MAC	ATQ	MAC
Abdallah et al. 2019	Egypt	Single-blinded RCT	General anesthesia	Anesthetist	35	35	$40.43 \pm 9.93$	$41.62 \pm 5.22$	19 (53.4)	22 (62.9)	34/35 (97.1)	33/35 (94.3)
Al-Ghamdi et al. 2016	Saudi Arabia	Single-blinded RCT	General anesthesia	Anesthetist	21	22	$34.5 \pm 10.43$	31.4 ± 8.96	10 (47.6)	8 (36.4)	9/21 (42.9)	16/22 (72.7)
Bhandari et al. 2013	India	RCT	General anesthesia	Anesthetist	40	40	$38.30 \pm 16.51$	$38.97 \pm 13.68$	14 (35.0)	10 (25.0)	NS	NS
Chalkeidis et al. 2010	Greece	RCT	General anesthesia	Anesthetist	35	28	$36.4 \pm 16.4$	38.5 ± 17.2	NS	NS	31/35 (88.6)	27/28 (96.4)
Çolak et al. 2015	Turkey	RCT	General anesthesia	Anesthetist	46	49	$47.7 \pm 16.86$	$49.69 \pm 16.04$	23	25	46/50 (92%)	49/50 (98.0)
Ertürk et al. 2015	Turkey	RCT	Surgery and General anesthesia	Anesthetist	40	40	38.5 ± 15.0	$40.4 \pm 13.7$	25 (62.5)	26 (65.0)	33/40 (82.5)	37/40 (92.5)
Ferrando et al. 2011	Spain	RCT	Any kind of surgery	Unskillful anesthesiology residents	30	30	NS	NS	NS	NS	20/30	24/30
Hindman et al. 2014	USA	RCT cross-over	Elective surgery	Anesthetist	14	14	47 ± 20	47 ± 20	5 (35.7)	5 (35.7)	NS	NS
Hosalli et al. 2017	India	RCT	General anesthesia	Anesthetist	30	30	$33.37 \pm 12.07$	$37.37 \pm 11.32$	13 (43.3)	11 (36.7)	27/30 (90.0)	23/30 (76.7)
Koh et al. 2010	Korea	RCT	General anesthesia / CSI	Anesthetist	25	25	$45.5 \pm 7.9$	44.0 ± 9.4	9 (36.0)	9 (36.0)	24/25 (96.0)	10/25 (40.0)
Maharaj et al. 2006	Ireland	Single-blinded RCT	General anesthesia	Anesthetist	30	30	$43.8 \pm 16.8$	$41.1 \pm 16.9$	11 (36.7)	11 (36.7)	30/30 (100)	29/30 (96.7)
Maharaj et al. 2007	Ireland	Single-blinded RCT	General anesthesia / CSI	Anesthetist	20	20	43.6 ± 19.4	45.7 ± 16.4	8 (40.0)	9 (45.0)	20/20 (100)	19/20 (95.0)
Maharaj et al. 2008	Ireland	Single-blinded RCT	General anesthesia	Anesthetist	20	20	$51.7 \pm 14.6$	$50.2 \pm 18.2$	8 (40.0)	10 (50.0)	10/20 (50.0)	13/20 (65.0)
McElwain et al. 2011	Ireland	Single-blinded RCT	General anesthesia / CSI	Anesthetist	29	31	52 ± 19	58 ± 20	14 (48.3)	19 (61.3)	28/29 (96.6)	25/31 (80.6)
Nishiyama 2011	Japan	RCT	General anesthesia	Anesthetist	36	35	$57.9 \pm 9.9$	$54.3 \pm 8.5$	20	19	29/36	31/35
Vijayakumar et al. 2016	India	RCT	General anesthesia	Anesthetist	45	45	$35.88 \pm 11.25$	$34.17 \pm 10.66$	14	15	45/45 (100)	45/45 (100)
Zhao et al. 2014	China	RCT	General anesthesia	Medical students	74	75	48 ± 18	49 ± 17	33	27	54/74	26/75

Table 2. Adverse events reported in	n include	d studies				
Type of adverse event	No. of studies	No. of incidence in ATQ group	No. of incidence in Mac group	OR (95% CI)	p value	12 statistic
Blood staining of laryngoscope blade	2	1/64 (1.6%)	2/66 (3.0%)	0.49 (0.04, 5.61)	0.56	NA
Sore throat	3	40/96 (41.7%)	56/97 (57.7%)	0.23 (0.04, 1.20)	0.08	56%
Laryngosplasm	1	0/35 (0.0%)	1/35 (2.9%)	0.32 (0.01, 8.23)	0.49	NA
Hoarseness	1	0/40 (0.0%)	0/40 (0.0%)	NA	NA	NA
Dental injury	2	0/81 (0.0%)	0/82 (0.0%)	NA	NA	NA
Muscosal trauma	1	1/21 (4.8%)	6/22 (27.3%)	0.13 (0.01, 1.22)	0.07	NA
Lips trauma	1	5/21 (23.8%)	4/22 (18.2%)	1.41 (0.32, 6.16)	0.65	NA

ATQ — Airtraq laryngoscope; MAC — Macintosh laryngoscope; OR — Odds Ratio; Cl — Confidence Interval; NA — Not applicable

attempt at endotracheal intubation under general anesthesia conditions. In the meta-analysis, the efficacy of the first intubation attempt with Airtraq was higher than with direct laryngoscopy. This relationship was even more evident when intubated under manual in-line neck stabilization. Many articles indicate the advantage of video laryngoscopy over direct laryngoscopy when intubating patients with 'difficult' airways (i.e. tongue edema) or when there are limitations in the patient's position due to the use of cervical collars [29, 30], manual in-line stabilization [31, 32] or continuous chest compression during cardiopulmonary resuscitation [33, 34]. It is therefore advisable to use alternative intubation methods to Macintosh laryngoscope in such cases, which will increase the effectiveness of intubation as well as may shorten the time of the procedure. An additional problem observed with multiple endotracheal intubation attempts is the vicious circle phenomenon in which each subsequent intubation attempt increases soft tissue trauma — bleeding and swelling, leading ultimately to a situation described by the Difficult Airway Society (DAS) as 'can't intubate, can't ventilate' [35]. Then the only solution is cricothyrotomy or tracheostomy [36].

Rapid airway management including endotracheal intubation in both prehospital and operating theatre conditions is essential. The prolonged endotracheal intubation procedure may cause hypoxia and related damage to vital organs due to hypoxia. As Wozniak et al. indicate, intubation attempts should be limited to a maximum of 30 seconds. Prolonging the intubation more than 30 seconds leads to greater hypoxia and may contribute to increased neonatal morbidity, with no effect on success rate [37].

#### Limitations

There are some limitations in our analysis that deserve special attention. The first limitation is the fact that only randomized controlled trials are included in the study, but this type of study guarantees the highest quality of results. The second limitation is the inclusion of articles comparing only Airtraq vs. Macintosh laryngoscope. However, this was deliberate. In the further parts of the series of studies, the authors plan to conduct meta-analyses concerning other types of laryngoscopes.

#### **CONCLUSIONS**

This systematic review and meta-analysis revealed that ATQ can reduce the failed first intubation attempt, especially in cervical manual inline stabilization patients, and reduces the time needed to obtain airway management, but does not provide significant benefits on other adverse events associated with tracheal intubation. Further studies are needed to demonstrate whether severe adverse events are significantly different between the two devices.

Authors contributions: The authors' primary responsibilities were as follows: M.M. and L.S. developed the research question. M.M. and L.S., designed the study. M.M., J.S. and L.S. collected the data. M.M., J.S., and K.R. analyzed the data and interpreted the results. M.M. and L.S. wrote the manuscript. L.S. and J.S. handled tools and provided supervision.

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### IMPLEMENTATION OF EXTENDED CARDIOPULMONARY RESUSCITATION PROCEDURE IN IN-HOSPITAL CARDIAC ARREST: A PRELIMINARY SIMULATED STUDY

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#### ABSTRACT

**INTRODUCTION:** The survival rate of patients after in-hospital cardiac arrest (IHCA) is poor. The implementation of novel technologies to conventional cardio-pulmonary resuscitation (CPR) may improve clinical outcomes.

AIM: To evaluate efficacy of extended CPR (ECPR) performed by physicians in the simulated scenario of IHCA.

**MATERIAL AND METHODS:** High-fidelity simulations were performed in a simulation room equipped with a full spectrum of emergency devices. Earlier, the physicians (n = 60, five courses) participated in a threeday training in the use of extracorporeal techniques. Eventually, 12 participants were divided into 4-member teams that were involved in three stages (assessed in terms of duration and quality) of scenario such as 1. Advanced Life Support (ALS) activities; 2. preparation of the extracorporeal membrane oxygenation device (ECMO); 3. cannulation and activation of ECMO.

**RESULTS:** All teams completed successfully scenario within recommended time of 60 minutes (ranged from 33 min. 55 sec. to 37 min.) after IHCA. In details, decision to activate ECMO team was taken between 8 min. 45 sec. and 14 min. 15 sec of scenario, ECMO device prepared within 10 min. 5 sec. to 15 min. 30 sec. whereas peripheral vessels cannulated in 4 min. 14 sec. to 6 min. 10 sec. Of note, all evaluated times were the shortest for teams with decisive leaders.

**CONCLUSIONS:** Implementation of ECPR procedure is possible within recommended time after IHCA. It has also been shown that training with application of high-fidelity simulation techniques is of paramount importance in achievement and maintenance of ECPR skills, not only manual but also in effective communication.

KEY WORDS: in-hospital cardiac arrest, cardio-pulmonary resuscitation, extended cardio-pulmonary resuscitation, simulation, education

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#### **INTRODUCTION**

Management of patients after in-hospital cardiac arrest episodes (IHCA) is still a real challenge for medical staff all over the world. For years, personnel have been attempting to reduce their frequency, implement effective therapy of sudden cardiac arrest (SCA) as well as appropriate resuscitation care. These actions are to ensure the highest possible survival rate for hospital discharge. The reported incidence of IHCA has ranged between 1 to 6 patients per 1 000 hospital admissions [1-3]. Generally, they are elderly people with many concomitant diseases who usually manifest symptoms at the time of hospital admission. The IHCA case analysis showed that the most common initial rhythm of SCA was asystole/PEA (79.3-84.3%) but not VF/VT (15.7–20.7%) [2, 4]. These results correlate strongly with a poor survival rate of about 10 to 20% of IHCA patients, where only half of them survived with good neurological outcomes [3-5]. Despite the enormous progress in medical technology, and although many detailed analyses have been carried out and standards of management and treatment of IHCA subjects have been changed, a poor progression has not changed markedly for many years. Only single reports noted slight increase in survival rate to 22.4%, and decrease in the neurological disability index from 32.9% to 28.1% [4].

The development of technology and the implementation of procedures that complement the conventional techniques used in IHCA are aimed at improving survival. One of these is a sophisticated procedure of the extended cardio-pulmonary resuscitation (ECPR). It has been shown that ECPR, compared with the conventional CPR, increased coronary perfusion pressure, improved the effectiveness of defibrillation and the likelihood of return of spontaneous circulation (ROSC) [6, 7]. This procedure requires a lot of commitment at every stage of its implementation, and the subsequent stages must be closely related to each other. At the time of SCA, it is important to continue additional activities from a preparation of the ECMO device at the beginning, cannulation and starting perfusion at the end [8-10].

While analyzing the cases of OHCA and IHCA in terms of ECPR procedure implementation, a number of discrepancies can be found. The mean age of OHCA patients is usually lower than that of IHCA subjects [11]. They are random ones with a poor medical history. It is important, but not always possible, to determine exactly the time of SCA iden-

tification by witnesses of the event as well as CPR activities undertaken by them while assessing the potential no-flow time. On the other hand, IHCA patients are more likely to be burdened with comorbidities such as, lung diseases, hypertension, diabetes, chronic kidney disease, dyslipidemia and cancer. However, they are often monitored and stay in rooms with other patients, so early identification of SCA is more likely [10–12]. Thus, the time of providing assistance will be incomparably shorter than in OHCA, and in the case of the monitored patients it may be 1-2 minutes [13]. These data indicate that SCA patients during hospitalization are more optimal candidates for ECPR. Early SCA diagnosis, short no-flow times, and easy access to a specialized team and equipment may be associated with good survival rates after IHCA.

#### Aim

The aim of this study was to analyze and evaluate the ECPR performed by physicians of various specialties in the simulated scenario of IHCA. The critical points collected on the checklist were assessed in relation to the proposed ECPR for IHCA procedure (Figure 1).

#### MATERIAL AND METHODS

#### Simulation mannequin

The SimMan 3G mannequin (Laerdal Medical, Stavanger, Norway) was used for the implementation of the high-fidelity scenario with silicone tubes creating loops to simulate pressured blood vessels. [14, 15].

#### Simulated scenario preparation

The scenario was carried out in real time with the use of tools used to conduct advanced ALS activities and cannulation of vessels with the ECMO device. The teams implementing the scenario were physician of various specialties such as cardiology, anesthesiology, cardiac or thoracic surgery and emergency medicine — they never worked with or known each other before. Earlier, the physicians participated in a three-day training in the use of extracorporeal medical technologies in the life-threatening conditions due to acute respiratory and circulatory failure after exhausting conventional therapy. During the classes, ECMO veno-venous (V-V), veno-arterial (V-A) ECPR protocols were implemented with the use of dedicated equipment. The training did not concern ALS procedures. The analyzed simulation scenario was the final one, summarizing the entire training

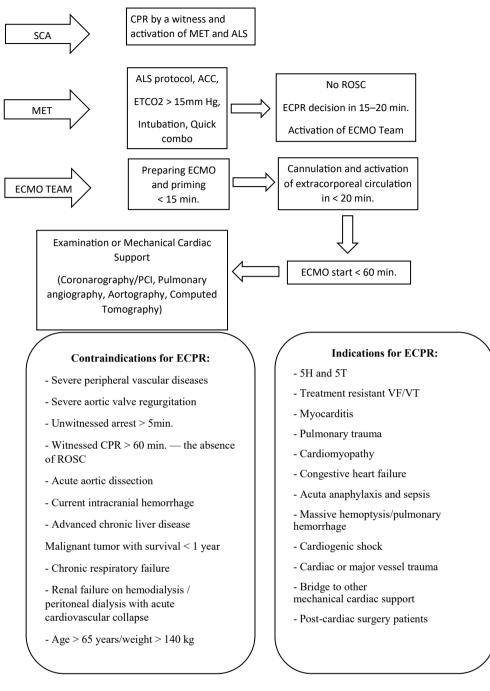


FIGURE 1. Proposed ECPR IHCA procedure

course. Before commencing the simulation, the participants were randomly divided into 3 four-member teams, regardless of the participants specialty. All study groups followed one identical scenario that was divided into three stages: I — ALS activities, II — preparation and priming of the ECMO, III — cannulation and activation of extracorporeal circulation. The scenario end time was set at 60 minutes in accordance with the assumptions adopted for the ECPR procedures. Each team individually performed its task in close cooperation with the others. Each stage of the scenario was assessed according to the previously prepared checklist (Table 1). Implementation of ALS was assessed in accordance with the adopted algorithm for defibrillating rhythms according to 2015 valid guidelines of ERC (European Resuscitation Council).

#### Simulation case scenario

In the scenario, SCA occurred in a 52-year-old male in the emergency room. While driving with his son, the father felt unwell and experienced shortness of

Table 1. IHCA scenario checklist						
	SCENARIO CHECKLIST					
1.	Time from touching the patient to diagnosis of SCA	Time				
2.	Initial rhythm recognition — time to first shock	Time				
3.	Advanced airway management	+/-				
4.	Maintaining high-quality chest compression and ventilation	+/-				
5.	Decision on drug therapy (1 dose of adrenaline and 1 dose of amiodarone)	+/-				
6.	Quick Combo decision	+/-				
7.	Time of use of ACC	Time				
8.	Analysis Time of each CPR cycle	Time				
9.	Decision on qualification for ECPR and ECMO therapy	+/-				
10.	Intubation time	+/-				
11.	ETCO2 monitoring	+/-				
12.	Taking into account the reversible causes of H and T	+/-				
13.	Assessment during resuscitation	+/-				
14.	Priming — total filling time	Time				
15.	Time of puncture of blood vessels from the femoral access; Cannula I, Cannula II	Time				
16.	Time to introduce the arterial and venous cannula	Time				
17.	Removal of clamps	Time				
18.	Time to start ECMO	Time				
19.	Time to stop ACC	Time				

breath and pain in his chest. This prompted the decision to drive to the hospital. During medical interview, the patient lost consciousness in the presence of witnesses. The Medical Emergency Team (MET) operating on the premises of the hospital was immediately activated. On arrival, the MET recognized SCA, implemented advanced ALS [including application of automatic chest compression device (ACCD)] and then informed the ECMO team. After arriving at the site, the latter one — without interrupting ALS — undertook preparations for vessel cannulation and began setting-up the device for extracorporeal circulation. The scenario end-point was the moment of starting the ECMO device and turning off the ACCD (ECMO Start/ ACCD Stop) (Table 2).

#### **Data presentation**

Due to a small number of performed scenarios (n = 5), the majority of continuous variables are

### Table 2. Medical staff/teams involved and equipment used in simulation of the ECPR scenario

Teams and equipment involved in the ECPR simulation scenario					
Teams					
Emergency staff 1					
MET 4					
Perfusion ECMO Teams 4 (cannulation), 4 (priming					
Equipment					
SimMan patient simulator (Laerdal Medical, Stavargen, Norway) with the ability of generating ECG rhythms, intubation, chest compression					
Handmade femoral vascular loop filled under pressure with red liquids, reproducing a system of vessels and implanted in the groin of the mannequin covered with subcutaneous tissue and artificial skin					
Advanced airway kit					
Cardiomonitor with electrotherapy capabilities					
1 x device for automated chest compression LUCAS (Lund University Cardiac Arrest System, Physio-Control Inc./Jolife AB, Lund, Sweden)					
Set of oxygenator a	and drains system				
Surgical set-up in the opera	ting room for cannulation				
ECMO — CARDIOHELP with he Germ					

presented as medians with range (minimal-maximal values) as they do not meet criteria of normal distribution. The only exceptions were some parameters of chest compression such as depth and rate that are presented as the means with standard deviations (SD). In a consequence of limited data, we did not to perform any statistical analysis to compare any data or to find any association between teams' composition (with respect to medical specialty) and results (i.e., quality of ALS actions, times of crucial points' completion, complications/mistakes).

#### **RESULTS**

Five ECPR for IHCA high-fidelity scenarios were carried out between October 2019 and October 2020.

#### **Basic life support actions**

The analysis showed that the median (range) time from the diagnosis of SCA to the final conclusion of the patient's initial rhythm was 31 seconds (range 9–50). It resulted in a significant extension of the time to the first shock where the median was 40 seconds (range 6–91). Only in one case was it within the recommended period of time.

The mean depth of chest compressions was  $4.5 \pm 0.5$  cm and the rate of compressions was  $85 \pm 10$  per minute. Each team used ACC and decision time to this device application varied from 2 min 10 sec. to 3 min. 46 sec. The time from defibrillation to the rhythm analysis ranged in individual loops from 2 min. 1 sec. to 5 min. All teams used Quick Combo electrodes and an ETCO<sub>2</sub> evaluation device.

## Extended cardio-pulmonary resuscitation techniques

An important element of the scenario was the decision to activate the ECMO team. Such decision was taken within the wide range from 8 min. 45 sec. to 14 min. 15 sec. after the beginning of cardio-pulmonary resuscitation. The teams responsible for preparing ECMO assembled the kit and primed it within 10 min. 5 sec. to 15 min. 30 sec. In the meantime, the other participants were involved in puncture of the vessel (femoral artery and vein) followed by insertion of the cannulas necessary for effective support. The cannulation was completed in 4 min. 14 sec. to 6 min. 10 sec. After connecting the arterial and venous cannulas, the teams activated the extracorporeal support that was considered as achievement of the end-point of simulation. All teams completed successfully complex high-fidelity simulation scenario. The time from first contact with the patient by the MET team to a valid flow of 4.5 L/min on circuit with ECMO device in V-A configuration ranged from 33 min. 55 sec. to 37 min. 30 sec. Of note, this period was the shortest if team leader was obvious and decisive.

The consequence of the implemented and analyzed in details high-fidelity simulation scenario was the preparation of a ready-made matrix of the high-fidelity scenario provided by the authors (Supplementary files).

#### **DISCUSSION**

In-hospital cardiac arrest is not uncommon. For example, in the United States alone, 292,000 adult patients are treated annually for IHCA with a relatively low survival rate of approximately 20%–30% [16–18]. The departments with the highest number of IHCA cases are intensive care, thoracic/cardiovascular and internal surgery [18]. The time from ad-

mission to hospital to the onset of IHCA was found to affect the survival rate that was markedly higher if IHCA occurred within the first 3 days than after 7 days of hospitalization [19]. The etiology of cardiac arrest also has influence on long-term survival. An analysis by Schluep et al. showed that the annual survival of cardiac-related IHCA patients was 39.3% whereas for non-cardiac patients it was only 10.7% [3]. The effectiveness of IHCA activities may also depend on the hospital profile. Mono-profile centers, limited by the number of cardiovascular specialists, are usually characterized by a higher mortality rate.

Many hospitals have established MET teams in their facilities, whose task is to quickly response to the deteriorating condition of the patient in order to prevent the occurrence of IHCA and to improve the treatment outcomes of patients in cardiac arrest. The exemplary critical vital parameters for activating the MET team include: heart rate > 150 or < 30 beats per minute, respiratory rate > 35 or < 8 breaths per minute, systolic blood pressure < 80 mm Hg, and blood oxygen saturation < 80% [20]. The role of such teams is of paramount importance since it had been found that in some patients clinical deterioration lasted several hours before the onset of IHCA. In one report, 40.0% of patients developed at least one serious abnormality 1 hour earlier, 31.1% at least 2 hours before cardiac arrest, and 13.4% of patients at least 4 hours prior to IHCA [20]. In another study, in almost 80% of patients with IHCA, vital parameters had already deteriorated 8 hours before SCA [21]. To improve the functioning and effectiveness of MET teams, their interdisciplinarity with a detailed division of roles, clear communication and training based on in situ high-fidelity simulations [22] are essential. In our study, a major problem at the stage of ALS activity was the lack of compliance with the time regimen in the algorithm for dealing with SCA in a defibrillating rhythm. It extended the time from defibrillation to analysis up to 5 minutes, as well as the time for drug delivery loops. The solution of such very likely problem may be the concept of a dynamic resuscitation team, where each team member is assigned to the specific role/s, and all actions are supervised by a leader. The role of a specialized team leader is to ensure that all activities are optimally coordinated and carried out on time. During ALS, there are always 6 mandatory roles/tasks to perform, such as 1. leader, 2. compressing chest, 3. caring of the respiratory tract (including ventilation), 4. monitoring, 5. drugs

Supplementary files.	Proposed high-fidelity scenario for ECPR	IHCA					
Main Medical Issue	Extended CPR, V-A ECMO Implantation — application of ECPR						
Educational aims	during resuscitation using the mechanica	d DCD n other ECMO team members n of the patient from the peripheral-femoral approach					
Brief case overview	son. While driving, the father felt unwell and to go to the hospital where the patient was r	D cm, transported to the emergency department by his began experiencing dyspnea and chest pain. They decided egistered and referred for observation. While interviewing tient lost consciousness. The paramedic who was with the began CPR					
Participants in the scenario	Medical Simulation Centre (MSC) staff Perfusionist, clinician, CSM employees (1 mannequin operation, 1 paramedic)	<b>Target group — training:</b> MET team 2–4 persons ECMO Team: cannulation 2–4 people, priming 2–4 people					
Location	Emergency department						
Mannequin — clothes and props	<ul> <li>Mannequin dressed in shirt, pants, under</li> <li>Mannequin with the possibility for intuba</li> <li>Assembled system simulating the patient with high pressure of artificial blood</li> <li>Injection kit, drugs, fluids</li> <li>Intubation kit, self-inflating bag</li> <li>Defibrillator</li> <li>ACC — mechanical automated chest com</li> <li>Cardiohelp pump</li> <li>Linear clamps — at least 4</li> <li>ECMO therapy kit compatible with Cardio</li> <li>1 venous cannula for femoral cannulation</li> <li>1 arterial cannula for femoral cannulation</li> </ul>	ation, monitoring, defibrillation 's vascular system placed (hidden) inside the mannequin npression device ohelp pump (head, drains, oxygenator) n with introducer					
Preliminary information for students (what they will see on the screen before the start of the scenario)	A monitored patient laying on the bed while a paramedic performs chest compressions The monitored rhythm — VF						
Initial vital signs of the mannequin	BP — not measurable No palpable pulse in large arteries No visible chest movement Cyanotic Pupils wide without reacting to light						
Initial ventilator parameters	Not applicable						
Initial pump parameters	None						
Initial monitor parameters for the measurement of saturation in the ECMO circuit	None						

managing and 6. recording/documenting. However, in case of limited availability of medical personnel,

some persons must play more than one role or be responsible for more than one task [19].

Supplementary files.	Proposed high-fidelity scenario for ECPR	IHCA				
Main Medical Issue	Extended CPR, V-A ECMO Implantation — application of ECPR					
Initial laboratory	Arterial blood gas: Electrolytes:					
values:	pH — 7.18 pO2 — 81 mmHg pCO2 — 63 mmHg Sat — 77%	Na — 151 mmol/l Ca — 1.22 mmol/l Cl — 105 mmol/l K — 5.1 mmol/l				
	Metabolites: Acid-base balance:					
	Lac — 9 mmol/l         HCO <sub>3</sub> - — 16 mmol/l           Glu — 410 mg/dl         BE — 19 mmol/l					
Other tests:	Not applicable					
Situation description, evolution of vital parameters of mannequin and parameters of ECMO apparatus	<ul> <li>son. While driving, the father felt unwell and began experiencing dyspnea and chest pain; hence, they decided to go to the hospital. The patient was registered and referred for observation. While interviewing and monitoring was attempted, the patient lost consciousness. The paramedic who was with the patient immediately called the MET team of which he is a member himself, and began CPR.</li> <li>MET:</li> <li>During this time the MET team should prepare for ALS activities. Divide roles among team members to implement ALS SCA algorithm in VF. During ALS with refractory VF, the MET team should consider launching the ECMO team — min. 15 minutes without ROSC.</li> <li>The VF rhythm is maintained throughout the course of the scenario.</li> <li>If the patient is intubated and ETCO2 is connected, the value should be:</li> <li>manual chest compressions, ETCO2 approx. 10 mmHg</li> <li>in the case of ACC ETCO2 &gt; 15 mmHg</li> <li>ECMO TEAM:</li> <li>PRIMING</li> <li>assembling, filling, preparing the ECMO device</li> <li>CANNULATION</li> <li>selection and preparation of equipment for the appropriate cannulation method including preparation of equipment and drugs for ECMO implantation</li> <li>preservation of sterility</li> </ul>					
Scenario ending versions	During ALS, the MET team encountering resis activate the ECMO team ECMO Team: Correctly prepares and primes ECMO device v Chooses the femoral cannulation method as the appropriate cannula (femoral vein and fer lidocaine — arterial spasm) within 20 minute If, from SCA through ALS, the initiation of the preparation of the ECMO apparatus, connect minutes — the scenario ends positively 2. NEGATIVE ENDING If, from SCA through ALS, VA ECMO initiation	POSITIVE ENDING: pper ALS carried out in accordance with ERC/AHA, using ETCO2, ACC ring ALS, the MET team encountering resistant VF makes the decision within 15–20 minutes to ivate the ECMO team <b>MO Team:</b> rrectly prepares and primes ECMO device within 15 minutes ooses the femoral cannulation method as the fastest access to VA ECMO implantation, prepares appropriate cannula (femoral vein and femoral artery) and drugs for implantation (heparin, local ocaine — arterial spasm) within 20 minutes from SCA through ALS, the initiation of the VA ECMO procedure, including cannulation of vessels, eparation of the ECMO apparatus, connection with cannulas and starting the VA ECMO within 60 nutes — the scenario ends positively NEGATIVE ENDING from SCA through ALS, VA ECMO initiation, vessel cannulation, ECMO apparatus preparation, nnection with cannulas and start of VA ECMO is longer than 60 minutes — the scenario ends gatively				

In-hospital cardiac arrest differs significantly from OHCA in term of both patient population and availability of new technologies [23]. Patients with IHCA are usually worse candidates for CPR/ECPR than OHCA patients. It was found that initial defibrillation rhythm among IHCA individuals was diagnosed more rarely than in those with OHCA (38% vs. 59%). If SCA occurs in hospital wards, it is highly possible that monitoring devices will be used, starting with ETCO<sub>2</sub>, through cardiomonitors, and ending with peripheral arterial and central venous catheters [24]. The use of the latter ones makes it possible to control cardiac output and index, the parameters that can predict early ROSC [24]. In the recent years, the availability of bedside echo-

able 3. Indications/contraindications and place of the ECPR procedure							
Indications for ECPR	Contraindications for ECPR						
Reversible causes of SCA: coronary artery obstruction, pulmonary embolism	Severe peripheral vascular disease						
VF/VT refractory to treatment	Severe aortic valve regurgitation						
Myocarditis	Unwitnessed arrest > 5min						
Pulmonary trauma	Witnessed CPR $> 60$ min. — the absence of ROSC						
Cardiomyopathy	Acute aortic dissection						
Congestive heart failure	Current intracranial hemorrhage						
Acute anaphylaxis	Advanced chronic liver disease						
Massive hemoptysis/pulmonary hemorrhage	Active malignancy with estimated survival $< 1$ year						
Poisoning	Chronic respiratory failure						
Sepsis	End-stage renal disease on hemodialysis or peritoneal dialysis with acute cardiovascular collapse						
Cardiogenic shock	age > 75 year						
Cardiac or major vessel trauma	weight > 140kg						
ECMO Site							
Bridge to another extracorporeal left ventricular assist device	Mobile team						
Patients before or after cardiac surgery (transplant)	Cardiac surgery intensive care units						
Patients before or after cardiac surgery	Heart catheterization laboratory						
	Cardiac surgery intensive care units						
	Operating theatre						

Table 4. Notes from the	Analysis of Individual Areas of the Si	mulation Scenario
Stage of ECPR	Problems/comments	Countermeasures
ALS	Late identification of the initial rhythm	Assessment of vital signs while assessing the rhythm on the monitor
	Delay in delivery of first shock	Charging the defibrillator to complete the shockable rhythm recognition procedure
	Instrumental opening of the airways (intubation) — no confirmation	Auscultation of the chest as the end of the intubation procedure
	Relatively poor quality of chest compressions and ventilation	BLS training, periodically repeated with the use of quality control mannequins
	Extended length of time to run ACC device	Training for doctors of various specializations on the use of ACC devices
	Exceeding the time for resuscitation loops	Division of roles in the team, the role of the leader, role of the recorder — documenting the time of individual activities
ECPR Activation	Within 15–20 minutes	Increasing awareness of the possibility of using the extended CPR When to go When not to go
Preparing the device for extracorporeal circulation	Difficulty assembling the extracorporeal perfusion device	Practical and manual training
Priming	Assessed: - preparation time - completeness of the apparatus Maximum priming time of 15 minutes	Practical and manual training: early filling of the device
Cannulation and activating extracorporeal circulation	Maintaining asepsis Heparin administration, Maximum time of 20 minutes	Practical and manual training

cardiography that can be used during cardiac arrest has also increased. It enables detection of reversible causes of SCA (cardiac tamponade) or identification of spontaneous movements of the heart muscle [25].

In some cases, if conventional CPR techniques are ineffective, ECPR may be a solution. In recent years and months (SARS-CoV-2 pandemic), the availability of ECMO devices in hospitals has increased significantly. The findings in the previous publications favor ECPR in terms of mortality over conventional CPR [26, 27]. Wang et al. showed survival to hospital discharge at the level over 30% [28]. A Brussels study revealed favorable neurological outcomes at 3 months, in 21% of SCA patients following ECPR vs. only 11% after conventional CPR. The long-term survival data after SCA also favors ECPR over conventional CPR [29]. ECPR activation seems to be more efficient in IHCA than in OHCA. Previous report stressed that availability of equipment and the ECMO team in hospitals enables earlier initiation of extracorporeal support in IHCA than OHCA conditions [11].

Without any doubts, ECPR is a complex procedure and multidisciplinary team must be involved. It is a safe and clinically relevant method if it is applied within appropriate time. A fast decision to start the ECPR procedure is of crucial importance. According to the recommendations, it should be activated in the absence of ROSC within 15 minutes from SCA occurrence. In our study all teams managed to initiate ECPR within recommended period of time. Of note, low-flow time (defined as between start of CPR to ECPR activation) strongly correlates with survival, and probability of hospital discharge is higher when a shorter CPR duration [29, 30]. Kim et al. showed that every 10-minute increase in the duration of lowflow increases mortality by 5% [5, 31]. Moreover, it was proven previously that ECPR is effective in reversible SCA if activated within 60 minutes. All our teams in the simulated scenario were able to connect mannequins to ECMO device in less than 40 minutes after SCA, which should be considered as perfect result. Of note, all physicians involved in ECPR were soon after ECMO course with simulation as a crucial form of education method to gain experience in extraordinary complex and sophisticated medical technology. Although it was not a subject of our study, it should be mentioned that age of ECPR candidates matters. Hirlekar et al. demonstrated in their study that the 30-day survival rate decreased dramatically with each decade over 70 years of life [32]. Therefore, ECPR is indicated for a selected group of SCA patients. However, there

are no specific criteria for indications and methods of patient selection, and consequently they may different depending on the hospital [31] (Table 3).

#### Limitation

The major limitation of our study is a relatively small number of scenarios. Due to obvious pandemic restrictions only five scenarios were implemented as a pilot study. The authors plan to complete between 15 to 20 scenarios in total. Thus, in a title of our study we did point that it was an initial experience. Although, center for medical simulation is very useful for achieving practical skills it does not reflect completely natural circumstances, particularly in emergent situations. The idealized conditions of IHCA are associated with the availability of an interdisciplinary MET, constant readiness of the team and equipment, proper organization and constant preparation of the device for extracorporeal circulation (Table 4). This fact could have impacted on perfect results of examined teams, in terms of time to make a decision to connect ECMO (low-flow one) and to ECPR activation.

#### **CONCLUSIONS**

Implementation of ECPR procedure is possible within recommended time after IHCA. In order to improve the survival rate of SCA patients, regular training for medical personnel is necessary. This should include BLS/ALS, extracorporeal perfusion setup and cannulation skills. It has also been shown that training with application of high-fidelity simulation techniques is of paramount importance for achieving and maintaining ECPR skills, not only manual but also in effective communication.

#### **ABBREVIATIONS**

IHCA — in-hospital cardiac arrest
OHCA — out-of-hospital cardiac arrest
CPR — cardiopulmonary resuscitation
ECPR — extended cardiopulmonary resuscitation
ALS — advanced life support
ECMO — extracorporeal membrane oxygenation
SCA — sudden cardiac arrest
ROSC — return of spontaneous circulation
MET — medical emergency teams
ETCO2 — end tidal carbon dioxide
ACC — automated chest compression
DCD — donation after circulatory death
BLS — basic life support

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## **EVALUATION OF PAEDIATRIC HEAD TRAUMA PATIENTS** WITH COMPUTED TOMOGRAPHY; THE REQUIREMENT OF COMPUTED TOMOGRAPHY IN CHILDREN WITH HEAD INJURY: A CROSS-SECTIONAL STUDY

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#### ABSTRACT

INTRODUCTION: In this study, we aimed to reveal the cranial computed tomography (CT) results of paediatric head trauma cases taken in our hospital and what clinical variables might be related to pathology in cranial CT

MATERIAL AND METHODS: Age, gender, glasgow coma scale (GCS), open or suspicious skull fracture, vomiting  $\geq 2$ , retrograde amnesia  $\geq 30$  minutes, the detailed mechanism of injury and CT findings (if CT is available) were evaluated.

RESULTS: 66 of the cases were female (35.7%) and 119 were male (64.7%). The ages of the patients vary between 0 and 16 and the average age is 6.76. 108 (58.4%) of the patients had admitted to the hospital with traumas resulted from falling. 33 (17.8%) of them were passengers of a four-wheeled vehicle and 15 (8.1%) were had been crashed with a four-wheeled vehicle.

CONCLUSIONS: In paediatric head traumas, falls and traffic accidents are in the first place and the measures taken in this regard should be increased.

KEY WORDS: head trauma, CT scan, pediatric trauma

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#### INTRODUCTION

Paediatric head injuries are still important today. It is one of the highest causes of mortality and morbidity in paediatric traumas and seen commonly despite the use of special facilities with developing technologies for children such as special playgrounds, protective equipment against potential domicile accidents, and

child safety seats providing the least damage during a traffic accident [1, 2]. Especially, in underdeveloped and developing countries, traumas are among the leading causes of death among the young population and more than half of these deaths result from head traumas [3]. In severe cases, head traumas with mortality up to 70% have been reported as

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150–200/100.000 between 1 and 14 years old, and 550/100.000 in the 15–24 age group. Most of these head traumas (89.1%) are minor head traumas [4–6].

Computed tomography (CT) is recommended as the first imaging method to be performed in patients with severe head injuries without discrimination of children or adults [1]. In minor head traumas, it is recommended only in the selected patient group due to its cost and high dose radiation exposure [2, 7]. In the group of patients with minor head trauma, the rate of detection of pathological findings in cranial CT is between 4–8%, and only a small part of these pathologies results in mortality. However, despite these scientific explanations, physicians keep the cranial CT imaging threshold recommended in the guides low due to fear of malpractice, unwillingness to take a risk and easy accessibility [8, 9].

In this study, we aimed to reveal the cranial CT results of paediatric head trauma cases taken in our hospital and what clinical variables might be related to pathology in cranial CT. We gathered all the findings under a single roof, as malpractice cases may exist even in the mildest and the least life-threatening pathologies seen in cranial CTs.

#### **MATERIAL AND METHODS**

The medical records of 185 paediatric patients who were 16 years of age or younger with head traumas admitted to a secondary care center from June 2016 to December 2016, were assessed. Age, gender, glasgow coma scale (GCS), open or suspicious skull fracture, vomiting  $\geq$  2, retrograde amnesia  $\geq$  30 minutes, the detailed mechanism of injury and CT findings (if CT is available) were evaluated. All head CT scans were performed based on the combined decision reached by at least one general practitioner and one emergency specialist in the ER. This study was approved by the institutional ethics committee, which waived informed consent owing to the retrospective study design.

All statistical calculations were performed with SPSS 23.0 (SPSS for Windows, Chicago, IL, SA). The continuous variables were expressed as mean  $\pm$  standard deviation and the categoric variables were defined as percentages (%).

#### RESULTS

Our study included 185 paediatric head trauma patients admitted to our hospital on the specified

Table 1. Injury mechanisms of the patients				
	Frequency	Percent		
Driver in motor vehicle (4 wheels)	1	0.5		
Occupant in motor vehicle (4 wheels)	33	17.8		
Pedestrian stuck by motor vehicle (4 wheels)	15	8.1		
Pedestrian struck by motorcycle (2–3 wheels)	2	1.1		
Fall accident	108	58.4		
Assault (by fist, push or shake)	7	3.8		
Assault by hard object	6	3.2		
Hard object fallen onto head	3	1.6		
Head crash onto hard object	6	3.2		
Animal attack	4	2.2		

Table 2. GCS scores and pathological findings ratio in CT scan			
	CT scan + for pathological finding	CT scan — for pathological finding	
GCS 15	60 (33%)	102 (67%)	
GCS 13–14	11 (100%)	0 (0%)	
GCS < 13	12 (100%)	0 (0%)	

CT — computed tomography; GCS — glasgow coma scale

dates. Of these patients, 66 were female (35.7%) and 119 were male (64.7%). The ages of the patients vary between 0 and 16 and the average age is 6.76 (standard deviation is 4.359).

Of those patients, 108 (58.4%) had admitted to the hospital with traumas resulted from falling. 33 (17.8%) of them were passengers of a fourwheeled vehicle and 15 (8.1%) were had been crashed with a four-wheeled vehicle. Those were the most frequent three reasons of hospitalization. Injury mechanisms of the patients are classified in Table 1.

Pathology was detected in cranial CT in all (n = 23) paediatric head trauma patients with Glasgow Coma Scale 14 and below. In the patients that GSK was evaluated as 15, the rate of detection of pathological findings was GKS 13–14 and was found to be significantly lower than those with and GKS < 13 (p < 0.001). However, in 33% of patients evaluated clinically as GKS 15, appearance pathological findings in cranial CT is a point that should be emphasized (Table 2).

In all of the patients with open skull injuries (n-2), vomiting (n-17) and suspected skull fracture (n-8),

Table 3. Clinical findings and CT imaging rates of the patients					
	CT (+)	CT (-)	P value		
Open skull fracture (-) (+)	81 (44.3%) 2 (100%)	102 (55.7%) —	0.200		
Vomiting (-) (+)	66 (39.3%) 17 (100%)	102 (60.7%)	< 0.001		
Suspicious skull fracture (-) (+)	75 (42.4%) 8 (100%)	102 (57.2%) —	0.001		
Retrograde amnesia > 30 min (-) (+)	55 (35.5%) 28 (93.3%)	100 (64.5%) 2 (6.7%)	<0.001		

CT — computed tomography

pathological findings in cranial CT was detected. However, in open skull injuries, there was no statistical difference between the patients with pathology on cranial CT and the group without detection (p: 0.2). There is a statistical difference between patients with vomiting and suspected skull fracture and patients with pathology in cranial CT and those not detected (p; < 0.001 and 0.001, respectively). In patients with vomiting and suspected skull fracture, there is a statistical difference between patients with and without pathology in cranial CT (p; < 0.001 and 0.001, respectively). Retrograde amnesia was detected in 30 patients and 28 (93.3%) of these patients had pathological findings on cranial CT and there was a statistical difference between both groups (p; < 0.001). In addition, when retrograde amnesia is evaluated with other findings, the rate of vomiting was found to be higher in patients with retrograde amnesia (p = 0.03).

Clinical findings and CT imaging rates of the patients are presented in Table 3.

When patients were separated by two age limits, the rate of pathological findings in cranial CT was found to be similar between those below 2 years old and those above.

#### DISCUSSION

In the world also by including the developed countries, traumas are one of the most common causes of mortality and morbidity [10]. Among traumas, the head trauma is only itself responsible for 1/3 of mortalities. In our study, in the children with the head trauma, the ratio of the boys to the girls was found to be 1.8/1. This rate is lower than that of adults which were observed as 2.49/1-2.57/1 [11]. Boys are more active and keen on dangerous games and activities compared to the girls, which can explain this difference. The growing gap of the difference in the advanced age period is explained by a more active lifestyle, more work in the heavy industry due to industrialization and more presence in an open environment [11]. The most common complaint among our patients is a motor vehicle accident and falling. Admission reasons of our patients show similarity to the cases in the literature [12]. However, assault, which takes the third place as the cause of head traumas in adults, forms a very small part in paediatric head trauma [13]. This is because assault is more frequently seen in the adult patient group. The fight in the paediatric patient group is generally seen as pushing. It is common for patients with open skulls to have pathology in cranial CT. In the presence of a visible cranial pathology, cranial CT imagining is to investigate the presence of another pathology that is not visible below [14, 15]. We think that there does not exist any difference between the patients that pathological findings were observed or not in the cranial CT statistically because this pathology was rarely observed in our patient group. In terms of head trauma, vomiting is an important finding and stimulates the clinician. In imaging guidelines for head traumas, vomiting depending on the number or not is considered an indication (16-18). In the study in which 19.920 paediatric patients were analysed, including studies examining paediatric head traumas such as PECARN, CATCH and CHALICE CDRs, vomiting showed the possibility of pathology detection in CT imaging around 44% [17, 19, 20]. The reason of being so high in our study is that vomiting was observed in the severe cases. Another explanation may be that nausea and vomiting in patients with minor head traumas were neglected. Amnesia finding is a finding that indicates the presence of pathology in patients with head trauma and is seen only itself in moderate-risk patients. Retrograde amnesia is important because it decreases the reliability in the patient's history of trauma and can also be a finding of brain damage and constitutes an indication for cranial CT imagining [21]. In our study, pathology was found in cranial CT in most of the patients with retrograde amnesia. This is compatible with the studies in the literature and the recommendations of the guidelines and supports cranial CT imagining in children having head trauma with retrograde amnesia alone itself [21]. Vomiting in patients with retrograde amnesia is statistically significant and normal for two findings of head trauma accompany each other. The clinician's suspicion following the anamnesis and the examination is a result of his experience, and this suspicion helps to diagnose many diseases. Findings such as a battle sign, raccoon eye or hemotympanum in head traumas have been shown to be related with a skull base fracture in the literature [14, 22]. Apart from this, physical examination findings such as staging of the skull are especially important in suspicion of abuse [22]. Pathology is an important result in cranial CTs taken in paediatric patients in head traumas, which are considered to be suspicious skull fractures after anamnesis and examination by physicians. The importance of taking amnesia and acquiring examination skills in the training of physicians has been demonstrated with this study. The detection of pathology in cranial CT results after head trauma in the age group under two years and above made us think that physicians should be vigilant in two issues [23]. First of all, the symptoms and findings of children under 2 years of age, who cannot speak or express themselves, should not be ignored or underestimated [21, 24]. Secondly, if cranial CT imagining is not or cannot be performed in children under two years old, the family should be informed in the most appropriate way and emergencies should be explained. Otherwise, both the increasing number of unnecessary hospital applications and malpractice cases are inevitable [12].

#### CONCLUSIONS

In paediatric head traumas, falls and traffic accidents are in the first place and the measures taken in this

regard should be increased. There are many guidelines used in paediatric head traumas, and findings such as low GKS, retrograde amnesia, vomiting, suspicious skull fracture and open skull are important. Attention should be paid to the signs and symptoms in children under 2 years old and physicians should be trained in anamnesis-examination.

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### VICTIMS OF TERRORISM-RELATED DISASTERS: EXPERIENCE OF A HOSPITAL ON THE BORDER OF IRAQ

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#### ABSTRACT

**INTRODUCTION**: We aimed to analyze the data of patients who were admitted to our emergency department (ED) because of terrorism-related injuries.

MATERIAL AND METHODS: We have retrospectively analyzed the patients who were admitted to a state hospital's ED with terrorism-related injuries between 01.01.2016 and 01.01.2018. The data about mechanism of injury, injured body part, Abbreviated Injury Scale scores, management, and outcomes: discharge from the ED, hospitalization to the ward, transfer to the operation room and/or intensive care unit, transfer to a tertiary hospital, the length of stay in the hospital, exitus, and re-admission were analyzed.

**RESULTS:** Of the 296 patients admitted, 93.9% were male and 6.1% were female, and 14.2% of the cases were children. Gunshot wounds represented 66.2% of the cases, whereas 33.8% of them had explosion injuries. Overall ED mortality rate was 15.5%. The mortality rate was higher in gunshot wounds. The most affected regions were the extremities, pelvis and external organs. Thorax injuries had the highest rate of mortality. Of the patients, 42.2% were discharged from the ED. The highest rate of ED discharge was with extremities, pelvis and external organ injuries. The ED mortality rate in the pediatric group was 21.4%. Gunshot wounded group had a higher mortality rate. Similar to adults the highest mortality rate was in the thoracic injury group.

**CONCLUSIONS:** Because of the variety of injuries, the management of terrorism victims requires a broad perspective. We think that the ED mortality rate can be used to assess the quality of the critical care provided.

KEY WORDS: emergency department, mortality, pediatric, terrorism

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#### **INTRODUCTION**

Terrorism is the physical and psychological act of violence that targets military personnel and innocent civilians; the goal is to cause dismay, consternation, murder, and mayhem for political or religious motivations [1, 2]. Turkey is the 14th most affected country in the world when it comes to the effects of terrorism; the country has experienced more than 5.000 deaths from terrorism between 1970 and 2013 [3, 4]. Terrorist attacks in the city centers mostly target civilians and mainly caused by firearm injuries, roadside bombs, and suicide bombers. In rural areas, these terrorist attacks are mostly war-like attacks against soldiers. However, the situation in our country differs. In these attacks, both military personnel in city centers and civilian people in rural areas can

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be targeted simultaneously. This variability in terrorism-related attacks has also changed the affected population over time. The population that is being affected by terrorism has changed over the years to include women and children, who are now the subjects of gunshot wounds (GSW) and explosions as well as men.

The injury mechanism is known to be a major defining factor of the clinical effects of the injury itself [5, 6]. For example, handmade explosives (HE) are widely used in terrorist attacks because of their low cost, but they cause more deaths and amputations than GSW because they can be enhanced with nails and metallic marbles [7]. Therefore, managing terrorism-related injuries must be given extra attention because of the broad-spectrum terrorism-related injuries fall under, including GSW, various types of explosion injuries, and even burns [8].

As the danger of mass casualties from terrorist attacks has increased worldwide, quality medical care has become an increasing concern [9, 10]. Considering that the first encounters with the victims of terrorism happen in emergency departments (ED), the analysis of previous cases and their patient populations, types, mechanisms of the injuries, and management strategies may help ED physicians make better decisions regarding differentiating critically ill patients, making rough risk stratifications, and transferring these patients to proper health facilities. Based on this, we aimed to analyze the data of patients who were admitted to our ED because of terrorism-related injuries.

#### **MATERIAL AND METHODS**

We have retrospectively analyzed 296 patients who were admitted to a state hospital's ED with terrorism-related GSW and HE injuries between 01.01.2016 and 01.01.2018. The hospital where the study was conducted is in a city Hakkari, on the border between Iraq and Turkey. During this period, both military personnel and civilian people were evaluated in the same emergency room.

The analysis included age variation, gender, mechanism of injury, injury site, abbreviated injury scale (AIS) 2005 scores, interventions, ED management, and outcomes which are: discharge from ED, hospitalization to the ward, transfer to operation room (OR) and/or intensive care unit (ICU), transfer to a tertiary hospital, length of stay in the hospital, exitus, and re-admission. The ED mortality rate has been specifically calculated in this study. The mechanisms of injury were considered in two categories: GSW and HE injuries. The frequency of organ injury was examined in the aspect of the criticality of the injury that mandated urgent intervention, the most affected system, and the injury that causes a life-threatening situation that led to causality.

These anatomic body regions affected by trauma were classified in a way similar to the calculation in AIS: head and neck; face; thorax; abdomen; extremities, pelvis and external organs.

The relation of the morbidity and mortality to these anatomic regions, in addition to interventions and management strategies (transfer to the ward, OR and/or ICU and discharge from ED), were investigated. In the first step, all data were analyzed before patients were divided into age groups. Patients between 0 and 18 years old were analyzed distinctly as a pediatric subgroup. In the second step, this pediatric group was examined separately. Also, it was examined whether the results of this pediatric group reflect the whole patient group.

Statistical analyses were made using IBM Statistical Package for Social Sciences (SPSS) for Windows, Version 20.0 (IBM Corp. Armonk, NY: USA. Released 2011). Definitive statistics and a standard deviation were calculated for the age variable, which was considered a continuous variable. Categorical variables were statistically analyzed with a chi-square test. Mann-Whitney U and One-Way ANOVA tests were used to compare independent groups. Logistic regression analysis was performed to examine the variables affecting mortality and hospitalization outcomes.

#### RESULTS

Of the 296 patients enrolled in the study, 93.9% (n = 278) were male and 6.1% (n = 18) were female. 61.5% (n = 182) of all patients were soldiers. The pediatric group represented 14.2% (n = 42, 33 male, 9 female) of the cases. The mean age of all civil patients was 25.9  $\pm$  10.5 and the mean age of soldiers was 26.8  $\pm$  6.9 (Figure 1).

According to the mechanism of injury, 66.2% (n = 196) of the cases suffered GSW, whereas 33.8% (n = 100) of the cases were subjects of explosion injuries. In the soldier subgroup, the injury mechanism was distributed as 79.7% (n = 145) GSW and 20.3% (n = 37) HE. The frequency of GSW injuries was higher in the soldier subgroup. This difference

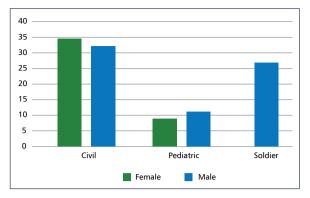


FIGURE 1. Distribution of patient groups by age and gender

was statistically significant (p = 0.000). There was no difference between children and civilian adults in terms of injury mechanisms.

The most affected anatomic regions in the overall patient population were the extremities, pelvis and external organs (p < 0.001) (Table 1). These rates were similar for civil and military personnel. In the pediatric subgroup, this ratio was the same, extremities, pelvis and external organs were the most affected body parts with a ratio of 57.1% (n = 24). This was followed by head and neck injuries (n = 8), thorax injuries (n = 6), abdominal injuries (n = 2) and face injuries (n = 2) with the ratio of 19%, 14.3%, 4.8%, and 4.8%, respectively.

When the mechanism of injury and the anatomical body regions were examined, a statistically significant relationship was found between them (p < 0.001). The injuries associated with GSW were observed in 81.4% of the head and neck, 80.6% in the chest and 81.2% in the abdomen. However, 66.7% of facial injuries were due to HE (Table 1). The distribution of these injuries in the military subgroup was; 88.9% head and neck, 90.5% chest and 100% abdomen (p = 0.006). Also, we found a statistically significant relationship in the pediatric group (p = 0.003). We found that 87.5% of head and neck injuries were related to GSW. And all of the facial injuries and 79.2% of the extremities, pelvis and external organ injuries were associated with HE.

The mean AIS score of all patients was  $2.73 \pm 1.50$ . AIS scores according to the affected anatomical regions were shown in Table 2. The mean AIS scores in head and neck, thorax and abdomen injuries were statistically higher than face and extremities, pelvis and external organs injuries (p < 0.001). A statistically significant relationship was found between the AIS score and mortality for

Table 1. The mechanism of injury and affected anatomical body regions (for all patients)					
	Injury mechanism				
	HE		GSW		Total
	n	%	n	%	n
Body region					
Head and neck	11	18.6	48	81.4	59
Face	20	66.7	10	33.3	30
Thorax	6	19.4	25	80.6	31
Abdomen	3	18.8	13	81.2	16
Extremities, pelvis, external organs	60	37.5	100	62.5	160

GSW — Gunshot Wounds; HE — Handmade Explosives; n — number

Table 2. Abbreviated injury scale scores of patients according to the affected anatomical regions					
	Anatomic region	n	Mean	SD	
AIS	Head and neck	59	3.4	1.79	
	Face	30	1.6	0.81	
	Thorax	31	4.4	1.63	
	Abdomen	16	3.9	0.99	
	Extremities, pelvis and external organs	160	2.2	0.96	

AIS — Abbreviated Injury Scale; n — number; SD — Standard Deviation

Table 3. Distribution of pediatric patients according to patient outcomes and length of hospital stay				
		Pediatric age groups		
	0-5 years n = 6	6–10 years n = 13	11–17 years n = 23	
Outcomes				
ED discharge	66.7%	61.5%	34.8%	
Transfer to ward	-	15.4%	21.7%	
OR and/or ICU	16.7%	15.4%	4.3%	
Tertiary center transport	-	7.7%	4.3%	
Exitus	16.7%	-	21.4%	
Length of hospital stay				
Mean, day	6	10.8	11.6	

ED — Emergency Department; GSW — Gunshot Wounds; HE — Handmade Explosives; ICU — Intensive Care Unit; n — number; OR — Operation Room

all patients (mean difference 3.37; 95% CI = 3.16–-3.581) (p = 0.000). Also, there was a statistically significant relationship between the AIS score and mortality in the pediatric group (mean difference 3.27, 95% CI = 2.76–3.78) (p = 0.000).

We analyzed that 42.2% (n = 125) of the patients were discharged from the ED, 17.5% (n = 52) were hospitalized in various wards, 16.8% of them (n = 50) were transferred to the ICU and/or OR, and 7.8% (n = 23) of the patients were transported to a tertiary center. The mean length of hospital stay for all patients was 12.1 (1–86 days). No significant difference was found between the patient groups in terms of hospital stay (p > 0.05). The length of hospital stay was similar in patients with GSW (52% hospitalized for longer than 7 days) and with HE (55% hospitalized for longer than 7 days).

In the pediatric group, 47.6% (n = 20) of the patients were discharged from the ED, 16.7% of them were hospitalized in the ward, 9.5% (n = 4) were transferred to the ICU and/or OR, and 4.8% (n = 2) of the children were transferred to a tertiary center. The mean length of hospital stay for pediatric patients was 10.3 (1–28 days). Overall pediatric ED mortality was 21.4% (n = 9). Mortality and length of hospital stay did not vary significantly between age groups of pediatric group (Table 3).

Overall ED mortality was 15.5% (n = 46). Forty patients (87.0%) were injured by GSW whereas 6 patients (13.0%) were injured by HE (p = 0.001). We have seen that 34.4% (n = 43) of patients with HE injuries were discharged from the ED. This ratio was 65.6% (n = 82) in patients with GSW (p < 0.001) (Figure 2). In the pediatric group, the ED

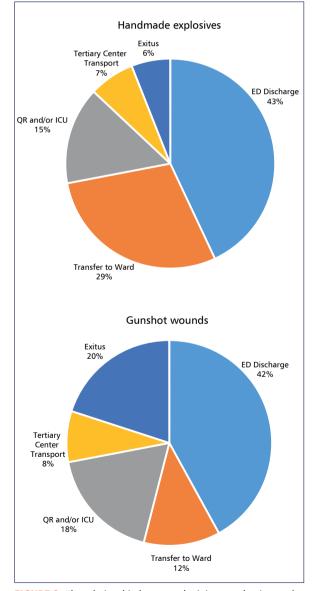


FIGURE 2. The relationship between the injury mechanism and the patient outcomes

mortality rate was 88.9% (n = 8) and 11.1% (n = 1) for GSW and HE, respectively. For patients suffered from HE, 85.0% (n = 17) were discharged from the ED (p = 0.003).

Looking at the relationship between the injured anatomic regions and the patient outcome for all patients the highest ED mortality rate was associated with injuries to the thorax (p < 0.001). Of the 31 patients who suffered thorax injuries, 20 (64.5%) died. This was followed by head and neck injuries with a ratio of 33.9%. The highest rate of urgent surgical interventions and subsequent ICU admissions was in patients with abdominal injuries, at a rate of 81.2% (13 out of 16 patients); the highest rate of ED discharge was in patients with extremities, pelvis and external organs injuries. Eighty-five of the 125 (68%) patients who were discharged from the ED were in this group. In the pediatric group, all patients with abdominal injuries had urgent surgical interventions. The highest ED mortality rate was in the thorax injury group (66.7%); in this injury group, 4 out of the 6 patients died. This was followed by patients with head injuries at 62.5% (5 out of the 8 patients). Also, there was a significant relationship between the injury site and outcomes in this group. When the pediatric group was excluded, the statistical results were similar in terms of injured anatomic regions and patient outcomes for the 254 patient group (p < 0.001).

Sixteen patients (5.4%) were re-admitted to the ED, and 32 patients (10.8%) visited various outpatient clinics within 30 days after initial admission. The re-admission rate was significantly higher in patients with GSW than with HE: 20.9% and 7%, respectively (p = 0.006).

Logistic regression models were used to examine the effect of age, gender, patient subgroup, injury mechanism, injured anatomic region, AIS and patient outcome factors on patient mortality and hospitalization. It was observed that these parameters had no significant effect on mortality. However, we found that three variables (soldier subgroup, trauma mechanism, and AIS) were effective in hospitalization. Being military personnel increased the probability of hospitalization (OR 0.30, 95% CI 0.15–0.62). Injury mechanism, i.e., HE, (OR 0.25, 95% CI 0.13–0.49) and high AIS (OR 1.59, 95% CI 1.18–2.13) also increased the probability of hospitalization.

#### **DISCUSSION**

Terrorism-related activities are spreading throughout the world. Over the past few decades, there has been a significant increase in global terrorism incidents [11]. In correlation with this increase, civilian casualties are also rising [12]. As per the literature that indicates that terrorism mostly affects young men, the vast majority of our patients were young men. The main reason for this could be that the security forces in the war zones are mostly men. Besides, these security forces are the first to respond to terrorist attacks that targeting civilians [13]. However, even when the soldiers were excluded from the analysis, we observed that male domination continued in accordance with the literature [14].

In the literature, pediatric trauma mortality rates in civilian-targeted terrorist attacks were found to be higher than for any other kind of pediatric traumatic injuries [15]. Children were twice as likely as adults (or adolescents) to present with severe injuries in terrorism-related activities [16]. In our study, 14.2% of the patient population was under the age of 18. In accordance with the literature, we found high mortality rates in the pediatric population above 10 years of age. Unfortunately, the total pediatric mortality rate in our study was two times higher than in the literature.

Peleg et al. reported that GSW usually presents with moderate-level injuries, whereas explosion injuries are more associated with a high rate of mortality [17]. The authors also stated that both types of injuries have similar in-hospital mortality rates, but the length of stay in the ICU for explosion victims was longer than GSW victims. Unlike Peleg et al., we noticed that most of the victims who died were associated with GSW, and explosion victims were frequently hospitalized in the ward. Similar to the adult group, GSW victims had a higher rate of mortality in the pediatric group, whereas most of the patients with explosion injuries were discharged from the ED.

In our study, the victim's extremities, pelvis and external organs were the most affected anatomic regions, which is in line with the literature [18, 19]. This was followed by head and neck, thorax, face, and abdominal injuries. In contrast with other injured regions, most of the patients with extremities, pelvis and external organ injuries were safely discharged from the ED. We acknowledged that the highest mortality rate was associated with thorax and head and neck injuries [20]. This is logical, considering that this region holds the heart, lungs, and other major vessels. Although, in a study where Amir et al. examined pediatric terrorism victims in Israel, the authors reported the highest mortality rate was associated with traumatic brain injuries; in our study, the highest mortality rate was linked to thorax injuries, which was similar to the adult group [15]. We assume that the mechanism of injury plays a definitive role in reaching the rate of mortality in the pediatric group. Most of the pediatric patients are injured while playing with a bomb setup or unexploded automatic rifle ammunition. Thus, these types of injuries mostly happened close to the victims' bodies.

Trauma scoring systems are systems that can help predict trauma severity. Abbreviated Injury Scale, which was used in this study, was an anatomic scoring system and we found that high scores were associated with high mortality [21].

The ED mortality rate was 87% for GSW and 13% for HE in our study. This may be because of the bimodal distribution of the blast injuries. According to the data obtained, if a victim survives an explosion, he or she is guite likely to be discharged from the ED and with a lower rate of ED mortality. In addition, the fact that Emergency Health Services frequently use the scoop and run technique in the explosion area may reduce the transport time and have an impact on mortality rates [22]. Another factor might be the evolved skills and experience of the ED personnel in years in managing this unique type of patient and coherent and exemplary collaboration with the emergency physicians, surgeons, cardiothoracic surgeons, orthopedists, and neurosurgeons as a trauma team in the ED.

We observed that re-admissions to the hospital were mostly in outpatient clinics. Avitzour et al. found that the mechanism of injury did not affect re-admission rates [23]. For the current study, readmission rates in patients with GSW were significantly higher than explosion victims. Thus, we may assume that the duration of recovery for GSW is longer than explosion injuries, and GSW are associated with far more degradation of the victim's quality of life. This situation creates an excessive cost burden and workforce loss to the economy when considered countrywide.

For the current study, there are various limitations. First, this was a retrospective cohort study. Second, we could only scan computer logs and tomography images. Thus, we could not obtain information about vital signs and important determinants, such as the Glasgow Coma Scale and Prehospital Revised Trauma Score.

We assumed that our sample size of 296 patients would be enough to achieve an appropriate statistical significance level when compared with similar reports in the literature [24]. For this study, we would like to highlight our concept of ED mortality. We defined this as the mortality rate in the period of the patient from the beginning of the admission to ED (door), primary and secondary evaluations, laboratory and screening studies, as needed, to the outcome (OR, ICU, in the ward, discharge, or exitus). We think that the ED mortality rate in terrorism-related patients may reflect the effectiveness and the ability of emergency departments in the well-directed management of these patients. We also believe that this may reflect the quality of critical health care in the ED.

Another prominent feature of our study was the analysis of the pediatric group, especially considering the rarity of the reports regarding pediatric terrorism-related injuries in the literature. We also could not find a report investigating the relationship between the mechanism of injury and the rate of hospital readmissions.

#### CONCLUSIONS

The ED management of terrorism-related injuries can be challenging because it requires a broad perspective. We think that the ED mortality rate in victims of terrorism may be a useful indicator when assessing the functionality and the skill of reacting to disarray in the emergency departments. It can also reflect the quality of the critical care provided in the ED.

**Conflicts of interest:** The authors declare no conflicts of interest regarding the publication of this paper.

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## **CLINICAL UTILITY OF EDACS-ADP IN PATIENTS ADMITTED WITH CHEST PAIN TO** AN EMERGENCY DEPARTMENT

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## ABSTRACT

INTRODUCTION: Acute coronary syndrome (ACS) is a common cause of mortality and morbidity. An ACS diagnosis can be made with electrocardiogram (ECG) and cardiac markers. However, despite medical advances, 2-5% of ACS patients are undiagnosed and discharged from emergency departments (EDs) because clinicians often find it difficult not only to diagnose and treat high-risk patients but also to define nonemergency diseases or safely discharge healthy patients. Risk stratification can be prevented, and inappropriate diagnosis and treatment protocols can be identified. The ED Assessment of Chest Pain Score-Accelerated Diagnostic Protocol (EDACS-ADP) scoring system, developed to identify patients with chest pain but at low risk for a major adverse cardiac event (MACE), is the first score based on clinical data from emergency medicine.

AIM: This study investigates the usability of EDACS-ADP in Turkey.

MATERIAL AND METHODS: This is a prospective observational study of 392 patients. The primary outcome was a major adverse cardiovascular event (MACE) within thirty days.

RESULTS: A total of 116 MACEs occurred in 65 (16,6%) patients during a one-month follow-up. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (+ LR), and negative likelihood ratio (-LR) values of the EDACS-ADP score for the evaluation of 30-day MACE rate in patients who admitted with chest pain for two months were as follows: 96.9%, 64.5%, 35.2%, 99.1%, + LR: 2.73, and -LR: 0.05.

CONCLUSIONS: Most of these patients were classified by the EDACS-ADP as low risk and suitable for discharge. The 30-day MACE rate of development was significantly low (0.9%) and acceptable in patients grouped as low risk.

KEY WORDS: chest pain, chest pain score, EDACS, ADP

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### INTRODUCTION

Chest pain is one of the most common complaints worldwide, requiring rapid, accurate diagnosis and

evaluation. In 3% to 6% of all emergency admissions, the only complaint is chest pain [1]. In the United States (U.S.), emergency services garner

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8-10 million visits per year due to chest pain, which is the second most common cause of admission and the number of annual ED visits is increasing [2-4]. Chest pain may be caused by non-life-threatening factors such as myalgia or by severe causes such as aortic dissection or pulmonary embolism. Although an ED evaluation usually focuses on serious pathologies, the last diagnoses in most patients are non-life-threatening causes. Acute coronary syndrome (ACS), pulmonary embolism, and aortic dissection are diagnosed in 12,5% of patients presenting to the ED with chest pain or discharged from the hospital after evaluation [5]. ACS, which is most commonly associated with chest pain, is a common cause of mortality and morbidity today. The diagnosis of ACS can be made by using ECG and cardiac markers; however, normal ECG and cardiac data do not mean the disease does not exist. Despite all the advances in medicine, 2-5% of patients with acute myocardial infarction (MI) are discharged from the ED without being diagnosed. These "missed MI" cases account for 40% of emergency service malpractice cases [6, 7].

For these reasons, when patients who have chest pain are evaluated in the ED, clinicians often find it difficult not only to diagnose and treat high-risk patients but also to identify non-emergency diseases or safely discharge those who have no disease. [8]. In patients who have chest pain, risk stratification can be prevented, and unnecessary diagnosis and treatment protocols can be identified. Also, lowrisk patients can be discharged from the ED quickly, reducing overcrowding and health costs [8, 9]. In contrast, the correct diagnosis of high-risk patients prevents premature discharge and allows these patients to be observed for longer times with all the facilities. For this reason, most current publications and guidelines recommend the use of a risk scoring system for patients presenting to the ED with chest pain [8, 10]. There are many scoring systems for evaluation of patients with chest pain or ACS, but most of them are designed to predict the potential for adverse events in patients undergoing intensive care or to distinguish patients at high risk from those with diagnosed ACS. Very few scoring systems are used for identifying low- to moderate-risk patients who may be discharged among those who present to the ED with chest pain [8, 9].

The ED Assessment of Chest Pain Score-Accelerated Diagnostic Protocol (EDACS-ADP) scoring system, which was developed to identify chest pain

patients with a low risk for MACE, is the first system based on clinical data from emergency medicine [9, 11]. The EDACS-ADP was created in 2014 by Than et al. [12], using information from patients who participated in the ADAPT study, and later validated in Australia and New Zealand, where it was developed. Researchers focused on two goals in developing the scoring system. The first goal was to develop a clinically reasonable score to predict the short-term risk of MACEs in adults presenting to the ED with a complaint of angina. The second aim was to accurately identify the low-risk group for MACE and to safely and guickly discharge them. Therefore, researchers developed the EDACS using a troponin assay and an ECG at the second hour and an accelerated diagnostic protocol (ADP) feature [12]. The EDACS-ADP can correctly classify more than half of those admitted to the ED with chest pain (51%) as low risk for MACE, allowing for early discharge. The rate of MACE development at the end of the thirty days after early discharge was 0.3% [8, 9]. Since its development, the EDACS-ADP has been validated by many prospective and retrospective studies in different countries. This study aims to investigate the usability of the EDACS-ADP scoring system as a risk stratification tool in Turkey.

### MATERIAL AND METHODS Study design and setting

This is a prospective observational study carried out on patients coming to the Ataturk University Hospital Emergency Medicine Clinic between 2/1/2017 and 3/31/2017. The diagnosis, treatment, and management of the patients included in the study progressed completely in accordance with the chest pain and ACS procedures in the hospital, and the discharge decision was made following these same procedures. The study was conducted independently of these protocols, and only the second-hour troponin value was measured from patients evaluated and recommended by a physician.

### **Study population**

The Ataturk University Hospital is a third-step public hospital. Located in Erzurum in Turkey it is the largest hospital in this province and operates an advanced diagnosis and treatment center for twelve provinces in its immediate vicinity. Approximately 120,000 patients are admitted to its ED annually, either by ambulance (112) or referral from hospitals in the surrounding provinces and districts. The hospital has a 24-hour coronary angiography laboratory with a team that is on-call during working hours and experienced in percutaneous coronary intervention (PCI). The dedicated biochemical laboratory for ED patients provides uninterrupted service throughout the day.

Patients over 18 years of age who were admitted to the ED with chest pain for more than five minutes and who read the consent form and agreed to participate were included in the study. The study included the troponin measurements taken in the ED. In the presence of any of the following criteria, the patient was excluded from the study: i. patients under the age of 18 years, ii. those who did not agree to participate in the study, iii. patients diagnosed with a certain reason for chest pain after initial examination without the need for further imaging and laboratory examination (e.g., thoracic wall pathologies, costochondritis, fibromyalgia, mastalgia, etc.), iv. patients with noncoronary pathologies as the cause of chest pain after imaging and laboratory tests (pneumonia, pulmonary embolism, pneumothorax, pericarditis, myocarditis, aortic dissection, GIS-induced pathologies), v. patients presenting with trauma-induced chest pain, vi. patients who did not think a cardiac test and follow-up necessary, vii. patients diagnosed with ST-segment elevation myocardial infraction (STEMI), viii. patients who were involved in the study before, ix. patients who did not have access to medical records, or who could not be reached after 30 days of follow-up, or who died due to cardiovascular reasons during the follow-up period, and x. patients developing cardiac arrest during evaluation in the ED.

#### Data collection

To record the patients' information, a study form was prepared in advance. This form was filled out by the study physician, who was not the patients' primary physician, by using the face-to-face interview method after evaluating patients in the emergency room, before the discharge or admission decision was made. Thus, the researchers were prevented from bias, and the study did not hinder the medical evaluation. A one-hour coordination and training meeting was held with the physicians who were likely to fill out the study form. Clinical symptoms and medical history were obtained by asking the patient directly, regardless of the medical records of the patient. If the patient was not sure of the answer (e.g., a history of hypertension), the answer was marked as "No."

### Calculation of the EDACS-ADP

More than three risk factors were identified for those aged 18 to 50 years: family history of premature coronary artery disease (CAD), dyslipidemia, diabetes, hypertension, current smoker, or history of seven heart diseases. Each of the variables has different negative or positive values according to its weight, and the total score is obtained by summing the values of the variables. The score of the two variables is negative, that is, when the scores of these precursors are collected, they are mathematically extracted from the total score. The result gives a patient score between -10 and 34. EDACS values above 16 indicate a high risk of MACE [10, 12, 13]. Table 1 shows the EDACS-ADP and the scores obtained from the variables [12]. If the EDACS is < 16 for a patient, if there is no new ischemic change in the ECG, and if both troponin values in the second hour are negative, this patient is considered low risk. Patients in this group may be discharged early in the outpatient period [12]. If the EDACS is > 16, or the ECG shows new ischemic changes, or if any of the troponin values are positive at the time of arrival or by the second hour, these patients are considered middle or high risk. If the initial troponin values are not taken, a delayed troponin test is performed [10]. For the EDACS, 16 is chosen as a cutoff because it maintains a sensitivity of 99% for MACE, while its specificity is maximum [10].

The patients' EDACS scores were calculated after discharge. Following the methodology for the EDACS-ADP derivation, a variable was considered normal or negative when calculating points during the study. In this way, while the study's reliability was maintained, the sensitivity was kept at the lowest obtained value, and, if the missing data were considered abnormal or positive, it was assumed that the sensitivity and specificity of the study would decrease [13].

### **ECG evaluation**

When a patient was admitted to the ED with chest pain, an ECG was performed within the first five minutes according to protocol. A copy of this ECG was kept with the study form and these results were evaluated in terms of new ischemia by two emergency physicians. If there was a difference between the physicians' ECG interpretations, a third blinded

Table 1. EDACS-ADP variables, variable points, and interpretation of the ADP program [12]			
Clinical features	Point		
Age 18-45 46-50 51-55 56-60 61-65 66-70 71-75 76-80 81-85 86+	+2 +4 +6 +8 +10 +12 +14 +16 +18 +20		
Male gender	+6		
Between 18 and 50 years old i. Known coronary artery disease* ii. More than three risk factors**	+4		
Sweating (diaphoresis)	+3		
Pain radiates to the arm or shoulder	+5		
Pain occurred or worsened by inspiration	-4		
Pain reproduced by palpation	-6		
Low-risk patient	All criteria must be provided 1. EDACS < 16 2. No new ischemia in the ECG 3. Negative series of troponin		
Risky patient	The existence of any criteria is sufficient 1. EDACS > 16 2. The presence of new ischemia in the ECG 3. Positive series of troponin		

ADP — accelerated diagnostic protocol; ECG — electrocardiography; EDACS — Emergency Department Assessment of Chest Pain Score-Accelerated Diagnostic Protocol \* Known coronary artery disease: a history of previous acute myocardial infarction, past coronary artery bypass graft surgery, previous coronary percutaneous intervention. \*\* Risk factors: family history of premature CAD, dyslipidemia, diabetes, hypertension, current smoker.

physician made the final decision. The ECGs of the patients included in the study were considered to have new ischemia in the presence of at least one of the following changes: i. at least 0.05 millivolt (mV) ST-segment depression in two or more adjacent leads and T wave inversion at a depth of ii. 0.1 mV or more (negativity), iii. a Q wave presence longer than 30 milliseconds and greater than 0.1 mV,  $\geq$  0.2 mV for leads V1, V2, V3 from iv. J point, an ST-segment height in at least two adjacent leads with a size of  $\geq$  0.1 mV, or v. a new left bundle branch block.

These changes were considered as old changes if present in the patient's old ECG or medical records. If there were no records to prove that the changes were old, they were evaluated as new ischemic changes. Data from the validation study of Flaws et al. [13] were taken as examples for this evaluation.

#### **Evaluation of troponin results**

The first troponin assay was done in the emergency room, and a second-hour troponin assay was performed on patients that the doctor was considering following. The serum troponin measurements were performed using a DXI 800 Beckman Coulter (U.S.) instrument. A troponin measurement of 0.04 microgram / L, which is the 99th percentile and above the reference limit, was accepted as the clinical threshold in determining myocardial injury during the study period. The EDACS-ADP was classified as high risk if there were values above this limit in the troponin measurements at the first or second.

#### Key outcome measures

The primary outcome was MACE. MACE development information was investigated by phone call and/or by examining the hospital records thirty days after the patient's discharge. If any of the following conditions developed over the thirty days, MACE formation was considered positive: i. acute MI (STEMI and NSTEMI), ii. emergency revascularization requirement, iii. cardiovascular death, iv. cardiogenic shock, or v. highgrade atrioventricular block or ventricular arrhythmia requiring access. Coronary artery bypass graft (CABG), stenting of the coronary artery, and other PCIs were considered as the necessity for emergency revascularization. MACE development was evaluated as positive in a patient who was admitted with chest pain after discharge from the hospital, not after discharge or hospitalization. For this reason, it was assumed that all NSTEMI patients developed MACE directly.

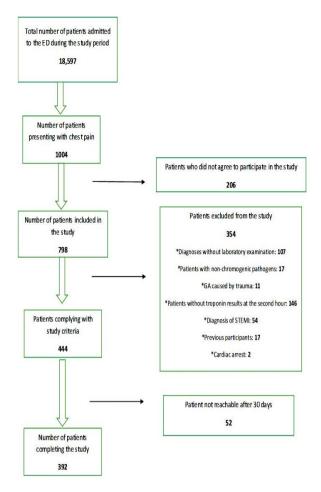
#### **Statistical analysis**

The SPSS 20.0 statistical software package was used for statistical analysis. Values were given with frequency, percentage, mean, and standard deviation. Pearson's Chi-square and Fisher's exact test were used to interpret the data. A Kolmogorov-Smirnov distribution test was used to examine the normal distribution, and a Mann-Whitney U test was used to compare the parameters between groups. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated according to the cutoff value. Results were evaluated at a 95% confidence interval and a significance level of p < 0.05.

#### RESULTS

A total of 18,597 patients were admitted to the ED. Chest pain was the most common reason for 1004 (5.4%) of these patients. Of these 1004 patients, 612 were excluded from the study due to various reasons, 206 patients refused to participate in the study, and 107 patients with chest pain complaints were discharged from the ED without any investigation after the first examination and were not included in the study. In this group of patients, the diagnosis was mostly chest wall pathologies. Since 54 patients were diagnosed with STEMI after the first ECG because of trauma-related chest pain, 146 patients were excluded due to the lack of troponin in the second hour after the clinician did not see the need for cardiac testing and follow-up. Seventeen of the patients had more than one visit with complaints of chest pain during the study period. The first applications of these patients were taken into consideration, while the other applications were excluded from the study. Two patients who developed cardiac arrest during ED evaluation were excluded from the study. Some of the patients were diagnosed with the non-coronary disease by laboratory and imaging tests. Seven of these patients were diagnosed with pneumonia, three with pulmonary thromboembolism, two with spontaneous pneumothorax, and two with myocarditis. One patient was diagnosed with pancreatitis, pericarditis, and aortic dissection despite chest pain. A total of 17 patients were excluded from the study. After 30 days of follow-up, 52 patients were excluded from the study. The study was completed with 392 patients (Figure 1).

Of the 392 patients who completed the study, 69.6% (n = 273) were male, and 30.4% (n = 119) were female. The mean age of the patients was 49.6  $\pm$  17.4 years (min: 18, max: 83). The vital signs of the patients included in the study are shown in Table 2, and their medical histories and cardiovascular risk factors are shown in Table 3. The median time after the onset of the patients' complaints was 240 minutes (IQR1: 120 min, IQR3: 900 min). There were new ischemic changes in the ECG of 52 (13.3%) patients. The arrival and second-hour troponin values of the patients who participated in the study were recorded and evaluated. The median





ED — Emergency Department; STEMI — ST-segment elevation myocardial infraction

Table 2. Vital findings of the patients included in the study					
Vital Signs	Average $\pm$ SD	Minimum	Maximum		
Systolic blood pressure [mm Hg]	135.98 ± 22.09	81	221		
Diastolic blood pressure [mm Hg]	80.91 ± 14.89	41	136		
Respiration [breaths/min]	16.42 ± 3.38	8	31		
Temperature [°C]	36.58 ± 0.41	35.4	39		
Fingertip oxygen saturation [%]	95 ± 3.41	81	100		

SD — standard deviation

value of arrival troponin was 0.00 mcg/L (IQR1: 0.00, IQR3: 0.006, minimum: 0, maximum; 16.71 mcg/L, mean: 0.27mcg/L  $\pm$  1.45); the median value was 0.00 mcg/L (IQR1: 0.00, IQR3: 0.007, minimum: 0, maximum: 24.23, mean value: 0.32 mcg/L  $\pm$  1.80).

## Table 3. Medical history of patients and cardiovascular risk factors

	n (%)
Known coronary artery disease	79 (20.2%)
COPD	28 (7.1%)
Heart failure	25 (6.4%)
Passed PKG	130 (33.2%)
Passed CABG	22 (5.6%)
Smoking	149 (38%)
Hypertension	102 (26%)
Dyslipidemia	57 (14.5%)
Diabetes	56 (14.5%)
Early coronary artery disease in the family	54 (13.8%)

COPD — chronic obstructive pulmonary disease; PKG — protein kinase G;

CABG — coronary artery bypass graft; n — number

Table 4. Distribution of patients with MACE			
MACE Reason	Patient No. (%)		
PCI (No MI)	8 (12.3%)		
NSTEMI	13 (20%)		
NSTEMI, PCI	37 (56.9%)		
NSTEMI, PCI, CABG	4 (6.2%)		
NSTEMI, PCI, CABG, high-grade AV block	3 (4.6%)		
Total	65 (100%)		

MACE — major adverse cardiac event; PCI — percutaneous coronary intervention; MI — myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infraction; CABG — coronary artery bypass graft; AV — atrioventricular

NSTEMI was diagnosed in 14.3% (n = 56) of the patients, USAP in 8.9% (n = 35), and nonspecific chest pain in 76.8% (n = 301).

A total of 116 MACEs developed in 65 (16.6%) of all patients included in the study during a onemonth follow-up. Of these 65 patients, 8 (12.3%) underwent PCI without troponin elevation (without MI). In 13 (20%), MACE was caused by NSTEMI alone, and no interventional procedures were performed. NSTEMI and PCI were associated with 37 (56.9%) patients. NSTEMI, PCI, and CABG were observed in 4 (6.2%) patients, and NSTEMI, PCI, and high-grade atrioventricular (AV) block were observed in the remaining 3 patients (4.6%). The distribution of patients according to MACE causes is shown in Table 4. NSTEMIs included in the MACE group were diagnosed in the ED. No patients developed MI after discharge. Of the patients who developed MACE, 59 were admitted to the cardiology clinic in the first ED. In 6 patients, MACE

Table 5. Frequency of EDACS determinants				
Clinical features	Score	n (%)		
Age 18-45 46-50 51-55 56-60 61-65 66-70 71-75 76-80 81-85 86+	2 4 6 8 10 12 14 16 18 20	175 (44.6%) 27 (6.9%) 36 (9.2%) 39 (9.9%) 25 (6.4%) 23 (5.9%) 15 (3.8%) 14 (3.6%) 2 (0.5%)		
Male gender	6	2 (0.5%)		
From 18–50 years old and I. Known coronary artery disease or II. More than three risk factors	4	29 (7.4%)		
Symptoms and findings				
Sweating	3	130 (33.2%)		
Pain radiates to the arm or shoulder	5	181 (46.2%)		
Pain occurred or worsened by inspiration	-4	105 (26.8%)		
Pain reproduced by palpation	-6	52 (13.3%)		
EDACS				
< 16		251 (64%)		
> = 16		141 (36%)		

 $\mathsf{EDACS} - \mathsf{Emergency}$  Department Assessment of Chest Pain Score-Accelerated Diagnostic Protocol; n - number

developed after discharge from the ED. While 81.5% of MACE patients were men, only 18.5% were women. This difference was statistically significant (p = 0.022 < 0.05). The mean age of the patients who did not develop MACE was 46.78 ± 16.98, and the mean age of patients who did develop MACE was 63.93 ± 11.95 years, and this value was statistically significant (p = 0.000 < 0.05).

Of the patients included in the study, 64% (n = 251) had an EDACS of < 16, while 36% (n = 141) had an EDACS > = 16. Further, 54.3% (n = 213) of the patients were classified as low risk according to the EDACS-ADP, and 45.7% (n = 179) were high risk. The frequencies of the EDACS determinants are shown in Table 5. MACE developed in 0.9% (n = 2) of the low-risk patients, while MACE developed in 35.2% (n = 63) of the high-risk patients (p = 0.000). According to these results, the sensitivity, specificity, PPV, NPV, + LR, and -LR values of the EDACS-ADP for the thirty day evaluation of MACE in patients who presented to the study clinic with chest pain for two months were as fol-

lows: 96.9% (95% CI 89,3–99.6%), 64.5% (95% CI 59.1–69,7%), 35,2% (95% CI 28,2–42,7%), 99,1% (95% CI 96.6–99.9%), +LR 2,73 (95% CI 2.35–3.18), and –LR 0,05 (95% CI 0.01–0.19).

#### DISCUSSION

To the best of the authors' knowledge, this is the first study conducted in Turkey on the EDACS-ADP system and one of the very few prospective studies on the EDACS-ADP in the world. Although there is no accepted consensus among clinicians on the rates of missed cases of MACE, many people think that a successful accelerated discharge protocol (ADP) should result in a MACE value of <1% in patients diagnosed as low risk. This performance would correspond to an NPV of 99% [11, 14]. In the presented study, the rate of missed cases among low-risk patients was 0.9% and the NPV value of the whole study population was 99.1%. In this regard, the use of the EDACS-ADP scoring system provides highly acceptable results in the population in which the authors are working. The rate of development of MACE was 16.6% in the study patient group. The rate was 6% in the study of Stopyra et al., 10.4% in Flaws et al., 15.4% in the derivation cohort, and 12.9% in the study of Than et al. [11–13]. Looking at MACE rates, the study patient cohort can be said to be at a higher risk, most likely because the study clinic is a part of the largest and best-equipped hospital in the area and therefore can accept more risky patients.

In the presented study, 54.3% of the patients were classified as low risk. In the EDACS-ADP derivation cohort and subsequent validation studies, this rate ranged from 41.2% to 66.7% [11-13]. In studies comparing the chest pain scores in previous emergency services, the EDACS-ADP is one of the best-rated scoring systems [15]. In the presented study, if the authors included patients with an EDACS of 12 or higher in the high-risk group, 41.3% (n = 162) of all patients would be in the low-risk group. In this case, no MACE would have occurred in the low-risk group. Thus, the sensitivity of the test would reach 100%, and its specificity would decrease to 49.5% with PPV and NPV values of 28.2% and 100%, respectively. This increases the power of the test for MACE estimation and reduces the rate of missed MACEs. Even though the EDACS-ADP system decreased the EDACS score to 12, making the EDACS-ADP more problematic to use for determining discharge, the EDACS-ADP allowed the decision to discharge more patients than many ADP tests under these conditions.

In the presented study, the authors found the EDACS-ADP concentrations to be 96.9%, while in previous studies, this ratio ranged from 88.2% to 100% [11–13]. In their validation study in the U.S., Stopyra et al. [11] found this to be lower (88.2%) than other studies and explained this as a result of the differences between the U.S. health system and that of other countries such as the more frequent use of angiography in the U.S. People in Turkey have a much higher rate of health insurance than in other parts of the world (98.6%) [16], and as a result, physicians can easily be found to perform interventional procedures. This may explain the relatively low sensitivity value found in this study.

The troponin kit used in this study was not highly sensitive. This raises the question of whether the use of high-sensitivity troponin alone will alter the diagnostic accuracy of the existing rules. However, unlike the original derivation and validation study using high-steroidal troponin, previous studies using traditional troponin did not look at the diagnostic performance of EDACS-ADP [13].

#### Limitations

the study results may not be generalizable as this study was conducted in a single academic centre, for only two months, and with relatively small sample size. The main criterion for inclusion was the presence of chest pain, which would exclude some patients with atypical symptoms, such as fatigue, nausea, and dyspnea but no chest pain. In this study, the EDACS-ADP could not be used to exclude conditions such as pulmonary embolism or aortic dissection, which are rare but fatal causes of chest pain. The patient's 30-day MACE development was obtained by guerying the patient or looking at the medical records, and if the medical records could not be accessed, the MACE status had to be obtained by phone. Although the assumption that the use of the EDACS-ADP system reduces hospital stays and decreases patient costs is theoretically correct, the cost analyses to prove this claim have not yet been done. Additional scientific data are needed to verify that patients have better outcomes when physicians use the EDACS-ADP method for differentiating chest pain causes than with current protocols.

#### **CONCLUSIONS**

Most of the patients who presented to the study clinic with chest pain were classified by the EDACS-ADP score as low risk and suitable for discharge. The 30-day MACE rate of development was significantly low (0.9%) in patients identified as the low-risk group and was acceptable. Therefore, this study showed that the EDACS-ADP scoring system as applied in a region different from previous study centres had comparable efficacy and safety.

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## IS USING METAPROTERENOL SULFATE RELIABLE IN HYPERTENSION MANAGEMENT DURING THE CORONARY ARTERY BYPASS GRAFT SURGERY **IN TERMS OF GRAFT PATENCY?**

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## ABSTRACT

INTRODUCTION: Coronary artery bypass graft (CABG) surgery that is a basic revascularization method is used commonly and hypertension appears frequently during and after CABG operations. In the treatment of hypertension, metaproterenol sulfate (MS) is one of the main agents; however, the effects of this agent on grafts are not known at an adequate level. The aim of the present study was to determine whether MS could be used safely in CABG operations by examining its effects on coronary grafts.

MATERIAL AND METHODS: This cross-sectional, prospective, experimental study was conducted at a university hospital. In this study, internal thoracic artery (ITA), radial artery (RA) and saphenous vein (SV) graft materials were studied in organ bath in patients who underwent CABG surgery between 2013 and 2016. In the organ bath, 10<sup>-6</sup> phenylephrine was added to the grafts to ensure that the ITA, RA and SV grafts contracted submaximally. Then, by adding MS with the cumulative method, the resulting relaxation results were recorded and dose-response curves were created. The p < 0.05 was considered as significant.

RESULTS: A total of 30 patients were included in the study. The average age of the participants was 59.3 (45-81) years. Minimum 1 and maximum 6 grafts (2.96 in average) were taken from all patients. Relaxation response was formed in the ITA at a rate of 40.49%  $\pm$  13.52, in the RA at a rate of 28.41%  $\pm$  9.08 and in the SV at a rate of  $23.87\% \pm 8.36$  by adding MS with the cumulative method. In the statistical work that was done by comparing the relaxation values among the SV grafts, ITA and RA grafts, it was determined that the efficacy of MS in the SV grafts was significantly lower when compared with the ITA and RA grafts.

CONCLUSIONS: In the present study, it was concluded that the risk of developing vasospasm was low in all three grafts when MS was used in intraoperative and postoperative periods. However, in the long-term, this made us consider that better graft patency rates might be obtained. Multicenter in-vivo studies with larger patient groups are needed to support our findings.

KEY WORDS: graft surgery, hypertension management, metaproterenol sulfate

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#### **INTRODUCTION**

In patients who have atherosclerotic coronary artery disease, methods such as stenting, balloon angioplasty and coronary artery bypass graft (CABG) surgery are known as the basic revascularization methods. CABG surgery was first used in late 1960s. The purpose in CABG operations is providing adequate blood-flow to the distal part of the heart vein where there is patency, providing blood to the ischemic myocardium in these areas, increasing the functional capacity of the patient by providing better contractions in myocardium, and helping to increase the life quality and life expectancy of the patient. Today, CABG surgery is used commonly.

A 42-year-old patient, who underwent coronary endarterectomy, received 'bypass' with saphenous vein (SV) grafts due to necessity. This anastomosis that was carried out by Johnson is considered as the first successful coronary bypass. After this period, the use of SV has become common. In the forthcoming years, the interest in it increased when it was shown that the patency rates of the internal thoracic artery (ITA) graft were higher than those of the SV grafts; and the use of ITA became 13% in early 1980s. In time, alternative arterial grafts were searched. Operations were performed in which other arterial grafts were used together with ITA, and complete arterial revascularization was obtained in this way. In our present time, ITA, radial artery (RA) and SV grafts are used commonly for CABG operations. One of the other grafts that may be used as autogenous grafts in CABG operations include gastroepiploic artery (GEA), inferior epigastric artery (IEA), splenic artery, subscapular artery, inferior mesenteric artery, lateral costal artery, and thoracodorsal artery [1]. In selecting the graft, the age and background of the patient, the location and spread of the involvement in coronary arteries, the condition of the vessel that may be used as the graft in the patient, and the opinion of the surgeon are influential. The structural and physiological characteristics of the graft that is employed in coronary artery 'bypass' operations have an important impact on the short- and longterm patency rates. If the graft spasm that occurs in the early period of the operation due to mechanical or pharmacological reasons is not resolved, it may affect the graft patency negatively in the short and long term [2]. For this reason, the effects of the pharmacological agents used must be well-known. For this purpose, the effects of the pharmacological

agents that are used must also be known well. For this reason, Green suggested papaverine injection to prevent spasm in IBA [3]. In case of necessity, proper relaxing agents may be administered to improve the graft blood-flow and to reduce the long-term patency rates by reducing the damage in the graft to the minimum level. It is known that the internal thoracic artery is the most commonly used graft due to its higher patency rates compared to venous grafts.

There is a medial layer, which is the excessive response to spasm by the RA. The spread of the RA use made it possible with the resolution of the vasospasm problem. Nowadays, it is the most frequently used arterial graft after ITA [6]. In many cases, RA can be removed safely as the ulnar artery provides sufficient blood-flow. However, anomalies like the lack of ulnar artery and incomplete SPA or SPA receiving blood dominantly from the RA might occur in this respect. For this reason, the collateral circulation presence must be evaluated prior to the RA graft use. In practice, this is carried out with the Allen Test [5].

Today, the major SV continues to be the most preferred method in coronary artery 'bypass' surgery with an ITA graft in many surgical centers [6]. The easy availability of the major SV as a graft, its easy removal, and its being resistant to spasm are considered as its advantages. On the other hand, it also has some disadvantages like low patency rates, diameter mismatch between the distal and proximal ends, varicosity, development of sclerosis, and especially in patients with peripheral arterial disease, the problems related to wound healing [7, 8].

Hypertension occurs frequently during and after CABG operations. The increased epinephrine and norepinephrine levels are held responsible for hypertension [9]. In the treatment of hypertension, metaprolol sulfate, esmolol hydrochloride, nitroprusside sodium and isosorbide mononitrate perfusions are known to be used as the main agents; however, the effects of these agents on grafts are not known at an adequate level. Metaproterenol sulfate has selective bronchodilator and beta mimetic effects. It is very effective in controlling the intubation, bradycardia and hypertension that occur in bypass surgery during catheterization. However, it must not be used for prophylaxis. The aim of the present study was to determine whether metaproterenol sulfate could be used safely in CABG operations by examining the effects of it on coronary grafts.

#### **MATERIAL AND METHODS**

This cross-sectional, prospective study was conducted at Namık Kemal University Hospital, Tekirdağ, Turkey. This University hospital has a capacity of 1042 beds. The daily number of application to cardiovascular surgery polyclinic is about 50 patients; and the annual number of patients undergoing CABG surgery is about 240. After the approval of the Ethics Committee of Namık Kemal University, Faculty of Medicine with the number NKUBAP.00.20. TU.13.02, and after obtaining metaproterenol sulfate that would be used in in-vitro organ bath by the team that was responsible for the study, the study was initiated. In this study, ITA, RA and SV graft materials were studied in organ bath in patients who underwent CABG surgery between January 1, 2013 and December 31, 2016 (3 years). Written informed consent was obtained from all the participants who were included in the study. The inclusion criteria of the study were being older than the age of 18, having undergone CABG surgery, being a patient with ITA, RA and SV graft materials, and being volunteers to participate in the study.

The CABG operation was performed in all patients who participated in the study by providing hypothermic CPB and cardiac arrest at NKUTF Cardio-Vascular Surgery Clinic. The ITA, RA and SV were used as graft in these patients. The internal thoracic artery was removed with pedicles with the help of electrocautery and scissors.

Titanium hemoclip was used to connect the side branches. The internal thoracic artery was cut after bifurcation. The superior epigastric artery (SEA) and the musculophrenic artery (MFA) branches in the distal area were clipped. The ITA part was taken without applying papaverine on the internal thoracic artery. In all patients, after the ITA was removed and prepared for anastomosis during the operation, the distal part that was removed was used. After the SV was removed with pedicles by dissection with scissors, the saphena was taken without inflating with SF. In selecting the RA graft, first the non-dominant arm was preferred; and the Allen Test was applied to the patients to evaluate the ulnar artery collateral circulation. The RA was not excised in patients who had RA cannulation history, subclavian patency, inadequate ulnar circulation, and who needed arteriovenous fistula for hemodialysis. After the radial-ulnar artery bifurcation discrimination, and following its removal in skeletonized form by clipping its side branches as of the wrist proximal area during the

operation, the remaining RA part was taken by dissecting it from the distal segment. The RA and ITA were excised with the help of cautery and scissors together with adjacent vein, fascia and surrounding fat tissue.

After the grafts were excised, they were not exposed to any vasodilator agents of any form during the preparation stage. Once they were prepared as graft, the remaining 1-cm parts of the ITA, RA and SV were taken into Petri dishes that contained +4°C Krebs Solution without any process. Then, they were brought to the laboratory at NKUTF Coronary Artery Surgery. The composition of the Krebs Solution (mM) was: NaCl 122, KCl 5; CaCl<sub>2</sub> 1.25; NaHCO<sub>3</sub> 25; MgSO<sub>4</sub> 1.2; KH<sub>2</sub>PO<sub>4</sub> 1.0; glucose 11.5. The grafts were dissected into 2-mm long sections by clearing the surrounding tissues in the light microscope at 22°C room temperature, and were suspended horizontally in the isometric transducer (FDT10-A, COM-MAT, Turkey) with a plating hook in organ bath that included 10 ml Krebs Solution aired with carbogene  $(95\% O_2 + 5\% CO_2)$  at  $37^{\circ}C$ ; and 2 gram pre-elongation was applied. The responses were transferred to the computer through 4-channel Transducer Acquisition System (COMMAT TDA-10-A, COMMAT, Turkey) and were recorded in POLWIN97 Program. For the adjustment of the tissues, washing was carried out every 10 minutes; the pre-elongation was set at 2 grams; and 90 minutes passed in this condition. To test the firmness of the vein endothelium, acetylcholine (10<sup>-6</sup> M) was administered to the prepared samples that were contracted submaximally with phenylephrine (10<sup>-6</sup> M) to test whether relaxation response existed. The samples that did not yield adequate relaxation response were excluded from the study.

The parts that were prepared at the beginning and at the end of the experiment were stimulated to receive their control responses. At the end of the experiment, in the control responses, the data that were obtained in the samples that showed significant amplitude reduction compared to the initial control responses at the beginning of the experiment were excluded from the analyses. To ensure standardization in the evaluation of the responses, all the responses were calculated over the percentage in the control traces that were obtained initially.

The metaproterenol sulfate (Boehringer Ingelheim-Alupent), which was purchased with the support of the researchers, and the potassium hydrochloride (Sigma) and phenylephrine (Sigma), which were already present at the Cardio-Vascular Surgery Department, were used in the experiment. The molarity calculations of these substances that were needed in the experiments were adjusted by weighing at precision scale (Mettler Toledo, AB 304-5). All the agents were prepared by dissolving them in distilled water. In the organ bath, the drug injections were applied with Eppendorf adjustable pipets (10–100  $\mu$ L, 100–1000  $\mu$ L). In the ITA, RA and SV samples, the dose responses of the metaproterenol sulfate were taken with the cumulative method, and the dose response curves were obtained. Then, the effects of metaproterenol sulfate were examined according to the responses received.

In the organ bath, 10<sup>-6</sup> phenylephrine was added to the grafts to ensure that the ITA, RA and SV grafts contracted submaximally. Then, by adding metaproterenol sulfate at rates that varied between 10<sup>-8</sup> and 10<sup>-4</sup> M (the cumulative method), the resulting relaxation results were rated to the relaxation with the phenylephrine contraction to create the dose-response curves.

#### **Statistical analysis**

The Graphpad Prism 6 program was used in the analyses of the data. The concentration-response graphics were obtained with this program that included statistical analysis in it. The non-linear regression analysis (variable slope) and the one-way ANO-VA were applied to the graphics. The p < 0.05 was considered as significant in statistical analyses.

#### RESULTS

A total of 30 patients, 15 (50%) of whom were males and 15 (50%) of whom were females, were included in the present study. The average age of the participants was 59.3 (45–81 years of age). The average age of the female patients was 60.6 (45–72), and that of the males was 58 (48–81). No statistically significant differences were detected between the genders in terms of age (p > 0.05).

Minimum 1 and maximum 6 grafts (2.96 on average) were taken from all patients. The number of the left ITAs that were taken as graft was 30; the number of RAs was 13; and the number of SVs was 25. No grafts were taken from the right ITA. The average partial by-pass time of the cases was determined to be 55.7 min. (27–110), and the total by-pass time was determined to be 86.2 min. (35–140).

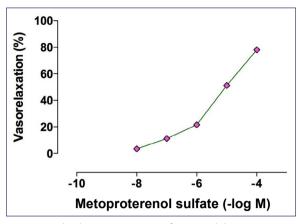


FIGURE 1. The dose-response curve for internal thoracic artery graft

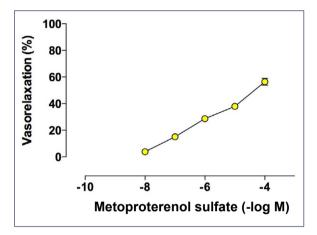


FIGURE 2. The dose-response curve for radial artery graft

Relaxation response was formed in the ITA at a rate of 40.49%  $\pm$  13.52 by adding metaproterenol sulfate with the cumulative method. By rating this relaxation to submaximal contraction, the relaxation dose-response curves were created for the ITA (Figure 1). With a similar method, the relaxation response in the RA was determined to be at a rate of 28.41%  $\pm$  9.08. The dose-response curve that was prepared for the RA graft is given in Figure 2. In the statistical work that was done by comparing the relaxation values between the ITA grafts and RA grafts, it was observed that there was no significant difference between the efficacy of metaproterenol sulfate on these two grafts (p > 0.05).

The rate of the relaxation that was caused in the SV as a response to metaproterenol sulfate that was added with the cumulative method was 23.87%  $\pm$  8.36. The dose-response curve that was created for the SV graft is given in Figure 3. In the statistical work that was done by comparing

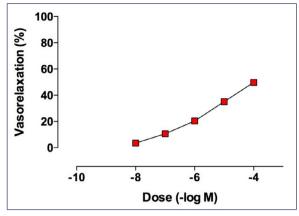


FIGURE 3. The dose-response curve for saphenous vein graft

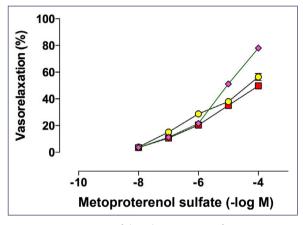


FIGURE 4. Comparison of the relaxation curves for in-vitro treatment with metaproterenol sulfate of internal thoracic artery, radial artery and saphenous vein grafts

the relaxation values among the SV grafts, ITA and RA grafts, it was determined that the efficacy of metaproterenol sulfate in the SV grafts was significantly lower when compared with the ITA and RA grafts (p < 0.05) (Figure 4).

#### DISCUSSION

Cardiac surgery has rapidly improved in the past 5 decades. The CABG surgery, which was mostly carried out with SV grafts, was preferred after 1980s because of the better long-term effects of the arterial grafts. The purpose is to provide adequate bloodflow to the ischemic area in the heart in bypass operations, which are used widely in our present day. The patency rates of autogenous grafts that are used for this purpose are related directly to the quality of life of the patient and the success of the CABG surgery. The patency rates in autogenous grafts are related closely with the damage on the endothelium during the removal process, and with the vasodilator agents employed in the postoperative period. The grafts that are used mostly in CABG operations are the ITA, RA and SV grafts [10, 11]. The grafts used in our study were the ITA, SV and RA grafts in line with the literature.

The idea that graft vasospasm might occur during CABG operations, and that this vasospasm might occur more in the RA caused that some surgeons had worries in this respect, which has become an important problem in the agenda [12]. The vasospasm in 'by-pass' grafts is associated with the damage to the vessel wall during removal and implantation. It is already known that the vasospasm is less in venous grafts. In studies conducted with SV grafts, the reason for this was claimed to be the extremely low- or even none- basal production or release of nitric oxide [13]. In arterial grafts, it was shown in previous studies that the nitric oxide release was higher than that in the venous grafts; and for this reason, the patency durations were longer. However, the thing that is important here is that if maximum care is not given during graft removal, nitric oxide production will decrease, and patency rates because of vasospasm will also decrease [14]. One of the most important reasons for early graft failure is the vasospasm [15]. Although the exact mechanism of vasospasm has not yet been clarified, ischemia, hypoxia and vasoconstrictor agents play important roles in the vasospasm mechanism. In addition, the increase in the surgical manipulation and vascular smooth muscle hyperactivity, biochemical and molecular factors as well as other factors [16], such as physical and pharmacological stimuli, are held responsible for this. It is possible that vasospasm occurs together with one or more of these factors [17]. As a result, perioperative morbidity, postoperative myocardial insufficiency and death may occur [18]. For this reason, the search has started for an agent that might prevent vasospasm. The effects of vasodilation agents on arterial grafts depend on the reason of vasoconstriction. If contraction is caused by potassium, which is a depolarizing agent, nifedipine and other calcium-channel antagonists are highly effective in achieving relaxation. The reason for this is that the depolarizing agent potassium causes contraction by ensuring that the calcium-mediated calcium channels are blocked by calcium antagonists. However, it is less effective in preventing the receptor-mediated contraction. For the first time in 1971, Green et al. reported that papaverine might be employed for this purpose; however, the search for other agents continued because it was not suitable for systemic use [3]. Papaverine has an effect on expanding blood vessels through multiple mechanisms of action, and is a non-specific vasodilator which is generally used topically. It is not suitable for systemic use because of its hypotension effect. It shows its real effect mechanism by increasing the intracellular cGMP level with phosphodiesterase inhibition [19]. It also acts by inhibiting the calcium intake to the cell and the secretion of calcium that is stored in the cytosol [19]. Thanks to this characteristic, it has been argued that it caused vasodilatation at a sufficient level in arterial grafts; and it is still used for this purpose in our present time [20]. The most important problem about the local use of papaverine is that it has a strong acidic structure. It was determined that it causes damage to the endothelial structure because of its strong acidic structure. While its topical application on adventitia layer is effective, its intraluminal use must be avoided because it might harm the endothelial structure. Nilia et al. reported that vasodilator agents might be required right after the removal of the graft [21]. Chanda and Canver reported in their studies that was conducted in 2001 that nitroglycerin might be employed in addition to agents like papaverine, nifedipine, verapamil, diltiazem that are all employed as vasodilator agents [22]. For this reason, organic nitrates such as nitroglycerin and sodium nitroprusside are currently used in CABG surgery. The mechanisms of action are known to increase the intracellular cGMP levels via the activation of guanylate cyclase in vascular smooth muscle cells depending on NO release. As a result, the levels of cytosolic calcium decreases, and relaxation occurs in the smooth muscle cells. In several studies that were conducted on arterial grafts, it was proven that they are effective vasodilators [23]. Among the calcium antagonists, which are divided into 3 groups according to their chemical characteristics, the calcium antagonist that has the weakest effect is known as the diltiazem [24]. As nifedipine, which is a more potent agent, does not have any intravenous form, verapamil and diltiazem are still being used [25]. Metaproterenol sulfate, which is one of the drugs that are employed in the management of hypertension, which appears before us during and after CABG surgeries, activates the adenylate cyclase, and provides dilatation by increasing the cAMP. However, no studies have been conducted on the effects of this drug on grafts. Selective beta-mimetic effective metaproterenol sulfate might accelerate the atrioventricular conduction, and increase the cardiac outflow, and therefore cause tachycardia and dilatation of coronary arteries. In our study, relaxation response was obtained in all grafts with metaproterenol sulfate. Among these grafts, the highest relaxation response was obtained with the IMA graft, and the lowest relaxation response was observed in the SV graft.

## **Study limitations**

The present study of ours has several limitations. The first limitation is the issue of whether the maximum relaxation that occurred due to metaproterenol sulfate because of high nitric oxide release in the ITA grafts mentioned in previous studies would be referred only to this drug or to the excessively-released nitric oxide. There is a need for studies at receptor level that will be conducted with endothelium and in de-endothelized fashion to clarify this issue. Aside from these, the limited number of patients, and the fact that the study was a single-centered one are other limitations of the present study.

### **CONCLUSIONS**

In the present study, when the relaxation rates that were formed on the ITA, RA and SV grafts after maximal contraction with the addition of metaproterenol sulfate with Cumulative Method was considered, it was concluded that the risk of developing vasospasm was low in all three grafts when metaproterenol sulfate is used in intraoperative and postoperative periods. However, in the long-term, this made us consider that better graft patency rates might be obtained. Multicenter in-vivo studies with larger patient groups are needed to support our findings.

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## ADVERSE REACTIONS OF COVID-19 VACCINATION: WHERE DO THEY COME FROM?

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KEYWORDS: COVID-19, vaccinations, adverse reactions, polyethylene glycol, anaphylaxis

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#### To the Editor,

Vaccination against SARS-CoV-2 is one of the most important elements to fight against the global pandemic of this virus. Implementation of the first vaccines against SARS-CoV-2 has been a breakthrough that may change the course of the pandemic. Concurrently, the first reports regarding the adverse reactions of vaccines have become available, raising concerns about the risk-to-benefit ratio.

In the study which investigated the efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine (Moderna) in 30.420 volunteers, the most frequent adverse effects in the study group included pain at the injection site (83.7% in the vaccine group vs. 17.5% in the placebo group), fatigue (37.2% vs. 27.3%), headache (32.7 vs 26.6%), myalgia (22.7% vs. 13.7%), arthralgia (16.6% vs. 11.8%), axillary swelling or tenderness (10.2% vs 4.8%), chills (8.3% vs. 5.8%), nausea and vomiting (8.3% vs. 7.1%), swelling (6.1% vs 0.3%), erythema (2.8% vs. 0.4%) and fever (0.8% vs 0.3%) [1]. At the median of 9 weeks after the second vaccine dose, serious adverse reactions were reported by 1% of the recipients in the vaccine group and 1% in the placebo group. These reactions included one Bell's palsy and two facial oedemas in patients previously undergoing aesthetic medicine interventions, suggesting allergic background. There

were no neurologic, thrombotic and inflammatory reactions.

Similarly, in the study evaluating the BNT162b2 vaccine (Pfizer) among 43.548 participants, the most commonly reported reaction was mild-to-moderate pain at the injection site. Pain was reported less frequently among older participants (> 55 years of age; 71% and 66% after the first and second dose, respectively) than among younger participants (83% and 78% after the first dose and second dose, respectively) [2]. The most commonly reported systemic events were fatigue and headache (59% and 52% after subsequent doses among younger recipients; 51% and 39% among older recipients). However, fatigue and headache were also reported by many placebo recipients (23% and 24%, after subsequent doses in younger participants; 17% and 14% among older recipients). Severe systemic events were reported in less than 2% of vaccine recipients after either dose. Fever defined as temperature  $\geq$  38°C was reported by 16% of younger vaccine recipients and by 11% of older recipients, with the temperature mostly below 39°C [3].

The Centres for Disease Control and Prevention (CDC) reported that there have been 21 cases of anaphylaxis after the BNT162b2 vaccine between 14 and 23 December 2020 (11.1 cases per 1 million doses), with 71% of them occurring within 15 min-

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utes following the vaccination [3]. Twenty of these patients (95%) were successfully rescued and only 1 patient died. The probable cause of anaphylaxis was polyethylene glycol (PEG), also called macrogol, which is an excipient and lipid facilitating the transport of mRNA-containing nanoparticles into cells and allowing for the synthesis of spike-protein — an antigen triggering immunity to SARS-CoV-2 [4]. PEG is an ingredient of multiple tablets, cosmetics and household products. Patients oversensitive to PEG usually had repeated systemic allergic reactions/anaphylaxis before diagnosis. Also, 81% of patients who experienced anaphylaxis after SARS-CoV-2 vaccine had known history of allergic reactions to medical products, supporting the hypothesis of allergic background underlying anaphylaxis.

Altogether, nearly 90% of patients experience any adverse reaction, compared to as much as 50% in the placebo group. The vast majority of these reactions are mild and resolve within 2 to 3 days. Serious adverse events are rare, and their incidence is similar in the vaccine and placebo group. The hitherto reported cases of anaphylaxis seem to results from oversensitivity to the excipients of the vaccine, rather than the vaccine itself. To summarize, the available evidence clearly shows that the benefits from vaccination substantially overweight the risks of COVID-19 disease, especially in the high-risk populations. Nevertheless, special caution should be taken in patients with established allergy to PEG, or a history of allergic reactions to other medications. Further research is required to evaluate the long-term efficacy and safety of the currently available COVID-19 vaccines.

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# MECHANICAL CHEST COMPRESSION DEVICES AS AN OPTION FOR OUT-OF-HOSPITAL CARDIAC ARREST IN COVID-19 PANDEMIC

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KEY WORDS: chest compression, mechanical chest compression, LUCAS, cardiopulmonary resuscitation, quality, survival rate, COVID-19, SARS-CoV-2

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We read with great interest an article by Malysz et al. [1]. In this manuscript, authors showed that over-the-head position is much more effective than standard position during chest compression. However, performing chest compressions while medical staff wears personal protective equipment (PPE) against aerosol generating procedure (AGP) may reduce the quality of resuscitation efforts. This is because of the heavy burden on medical personnel wearing PPE-AGP [2]. The above thesis is confirmed by many studies [3]. At this point, as indicated by another study by Malysz et al., it is worth considering chest compressions using mechanical chest compression systems [4]. Thanks to the use of this type of devices, we obtain full standardization of chest compressions. With travel teams, when they are limited to 2-3 people, it is even more important, because then the rescuer may focus on performing other medical procedures instead of compressing the chest.

A problematic in the COVID-19 era is a significant reduction in the survival rate of OHCA patients. Ball et al. [5] analyzing the data of the Victorian Ambulance Cardiac Arrest Registry showed that survival to hospital discharge in adult OHCA patients during COVID-19 pandemic period was 6.1%, while in the period before the SHD pandemic it was significantly higher and amounted to 11.7%. This relationship is also confirmed by the studies of Baldi et al., where SHD was 5.1% vs. 9.5% (p = 0.06) [6]. Importantly, in the studies indicated by Baldi et al. the frequency of mechanical CPR use was significantly lower for COVID-19 period compared to pre-COVID-19 period (respectively: 6.5% vs. 16.7%). In the study by Ball et al., however, it remained at a similar level: respectively 14.7% vs. 14.5% (p = 0.921).

In summary, it is justified in accordance with the guidelines of the European Resuscitation Council on Advanced Life Support during the COVID-19 pandemic to consider mechanical chest compression to facilitate transfer/treatment [7]. Due to the results obtained by Malysz et al., in favor of the use of mechanical chest compression, consideration should be given to the routine use of this type of device in relation to OHCA patients with suspected COVID-19.

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## SWOT ANALYSIS OF USE IN REMOTE MEDICAL EDUCATION PARAMEDIC DURING PANDEMIC COVID-19

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#### ABSTRACT

During the COVID-19 pandemic, academic education has assumed a different nature of work with a student. As medical teachers, we are obliged to look for new tools for working with academic youth who expect new ways of working remotely. Their advantage should be that they will be willingly used by the student and at the same time will be a measurable instrument for lifelong learning. This work presents new possibilities of using the SWOT analysis as a tool for working in academic conditions.

KEY WORDS: online education, medical education, COVID-19, paramedic

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In times of dynamic change, ever-present digitization, big data analysis and the development of artificial intelligence, some classical analytical tools have been forgotten or have been intentionally abandoned for strategic analysis. The COVID-19 pandemic has driven the fastest changes to higher education across the globe, necessitated by social distancing measures preventing face-to-face teaching [1, 2]. During the COVID-19 pandemic, we have suspended face-to-face curriculum-based classes with the students.

In order to adapt education to the current difficult situation, we had to launch all available knowledge for the proposed methods to be used in practice and to use the element of strategic planning and preparation of future medical staff for work in another crisis situation, e.g., a pandemic or a natural disaster. Besides, every academic teacher conducting teaching at the emergency medicine faculty, bachelor's degrees (N-76), (6th semester) was required to prepare a creative education plan for the period from March 15 to May 15, 2020. One of the solutions proposed by academic teachers was the use of the SWOT analysis, a popular heuristic technique for organizing and analyzing information [2–5]. The approach was taken that the SWOT analysis gives a valuable analytical result when taking each of the three mentioned approaches, provided that it is used consistently and consciously. The topic was: A patient with COVID-19 + in a life-threatening condition and a therapeutic team at the Hospital Emergency Department (SOR). The students received a link to the website (https://ptpaio.pl/?id=58) where the materials on COVID-19 were available. The hospital on whose example they were supposed to conduct an analysis was known due to previous

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seminars and practical training in which they underwent 240 contact hours under the supervision of a medical teacher and nurse teacher, nurse and paramedic instructor.

Strategic information included in the SWOT analysis, sorted into four groups, then stored in a four-fold strategic matrix, in which the left half contains two categories of positive factors, and the right half — two categories of negative factors, gives a valuable analytical result [2, 3, 5]. This allowed the teachers to assess the student's use of the available literature, familiarity with the ED, and the knowledge of the content planned in the syllabus, as well as the implementation of the intended learning outcomes in terms of knowledge, skills and social competences. Statistical analysis showed that 98%, 96% and 67% of the assumed learning outcomes were achieved respectively. Moreover, the assumed learning objectives for the analyzed form of education were achieved in 100%. The SWOT analysis is a popular heuristic technique about making discoveries, dealing with studying the laws that govern creative thinking, and the formation of the methods that facilitate and systematize this type of action.

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Dostęp do najlepszej wiedzy medycznej w ramach jednej prostej opłaty. Warto skorzystać już dziś!

# www.tvmed.pl