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ORIGINAL INVESTIGATION / ÖZGÜN ARAŞTIRMA

Pathological View of Cardiac Rupture and Myocardial Infarction

Kardiyak Rüptür ve Myokard Enfarktüslerine Patolojik Bakış

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ABSTRACT

Objective: This study aimed to investigate the cardiac rupture due to myocardial infarction. Differences between male and female sex, the most common age group, and the most common localization were investigated. In addition, we examined the dating of myocardial infarction at the site of the cardiac rupture and tried to determine the relationship between the age of myocardial infarction and cardiac rupture.

Method: Sixty cases of myocardial rupture at the Council of Forensic Medicine between 2015 and 2020 have been studied. Three cases with traumatic causes and two cases with inadequate information were not included in the study. The age, gender, height, weight, body mass index, localization of rupture site, presence of pericarditis, presence of fibrin thrombus in coronary arteries, presence of stents or artificial valve, and a known history of hypertension, diabetes, and bypass were noted.

Results: Of the 55 cases included in the study, 45 (82%) were males and 10 (18%) were females. The most common site of cardiac wall rupture was the left ventricular lateral wall (n=16, 29%). Twelve cases (22%) were histopathologically associated with pericarditis. Two cases (4%) have the presence of a stent in the coronary arteries. No cases have a history of bypass surgery.

Conclusion: In our study, the myocardial rupture was detected most commonly in the first 24 h of myocardial infarction that is followed by between the third and seventh day of myocardial infarction. The myocardial rupture was detected with older age. In addition, ruptures in women occur at a more advanced age than in men.

Keywords: Age, gender, localization, myocardial infarction, rupture, timing

ÖZ

Amaç: Bu çalışmada miyokard enfarktüsüne bağlı gelişen kardiyak rüptürünün araştırılması amaçlandı. Erkek ve kadın cinsiyet arasındaki farklılıklar, en sık görülen yaş grubu ve en sık yerleşim yeri araştırıldı. Ayrıca, kalp rüptürü bölgesindeki miyokard enfarktüsünün yaş tayini ve miyokard enfarktüsü yaşı ile kalp rüptürü arasındaki ilişkinin belirlenmesi de amaçlanmıştır.

Yöntem: 2015-2020 yılları arasında Adli Tıp Kurumu morg İhtisas Dairesi'nde 60 miyokard rüptürü olgusu incelenmiştir. Travmatik nedenleri olan 3 olgu ve yetersiz bilgi içeren 2 olgu çalışmaya dahil edilmedi. Yaş, cinsiyet, boy, kilo, vücut kitle indeksi, rüptür bölgesinin lokalizasyonu, perikardit varlığı, koroner arterlerde fibrin trombüs varlığı, stent veya yapay kapak varlığı, bilinen bir hipertansiyon öyküsü, diyabet ve bypass öyküsü kaydedildi.

Bulgular: Çalışmaya dahil edilen 55 olgunun 45'i (%82) erkek, 10'u (%18) kadındı. En sık görülen kardiyak duvar rüptürü bölgesi sol ventrikül lateral duvarıydı (n=16, %29). 12 olguya (%22) histopatolojik olarak perikardit bulguları da eşlik etmekteydi. 2 olguda (%4) koroner arterlerde stent varlığı saptanmıştır. Bypass ameliyatı öyküsü olan vaka saptanmadı.

Sonuç: Çalışmamızda miyokard rüptürü, en sık miyokard enfarktüsünün ilk 24 saatinde, ardından miyokard enfarktüsünün 3.ve 7. günleri arasında tespit edildi. Miyokard rüptürü ileri yaşlarda tespit edildi. Ek olarak, myokard rüptürleri kadınlarda erkeklerden daha ileri yaşlarda ortaya çıkmaktadır.

Anahtar kelimeler: Cinsiyet, lokalizasyon, miyokard enfarktüsü, rüptür, yaş, zamanlama

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INTRODUCTION

Free wall rupture of the heart after acute myocardial infarction was first described by Harvey in 1647.[1,2] In 1769, Morgagni, who ironically died as a result of a myocardial rupture, reported 11 cases of myocardial rupture discovered postmortem.[2,3] In some studies, it has been reported that Duaine published the first major series of patients with cardiac rupture in 1871, concluding that the rupture never occurred spontaneously.[2,4] However, the relationship between myocardial infarction and left ventricular free wall rupture was first pointed out in a report prepared by Krumbhaar and Crowell in 1925.[2,5]

Cardiac rupture is a catastrophic cause of cardiovascular death that causes a high rate and rapid death. Mortality in cardiac rupture was reported as 75–89%.[6–8] The incidence of cardiac rupture after acute myocardial infarction has decreased over the past two decades with the emergence of primary coronary intervention and the progression of drug therapy.[7,9,10] The incidence of cardiac rupture has been reported to range from about 1% to 3% after acute myocardial infarction, but autopsy research has shown that cardiac rupture is involved in 30% to 65% of in-hospital acute myocardial infarction-induced death.[9] This complication of acute myocardial infarction is more common in women, hypertensive patients, and patients who have had myocardial infarction for the first time over the age of 60 years, but these characteristics are not specific enough to identify patients at high risk of cardiac rupture.[11] Most cases of cardiac rupture in which the pericardium is intact are associated with blunt chest trauma or myocardial infarction.[6] Rarely, rupture can be caused by a complex interaction between trauma and cardiac diseases.[6] This is why determining the main causes of cardiac ruptures is extremely important for forensic pathologists.

The aim of this study was to investigate the differences between male and female sex, the most common age group, the most common rupture localization, and accompanying pathologies by examining deaths due to myocardial rupture in the Morgue Specialized Department of the Council of Forensic Medicine. In addition, the dating and time course of the myocardial infarction at the site of the cardiac rupture was examined and endeavored to determine if there was a relationship between the age of myocardial infarction and cardiac rupture.

METHOD

For the study, approval was obtained from the Council of Forensic Medicine Scientific Committee on June 21, 2021, with the number 21589509/855. Sixty cases of myocardial rupture at the Council of Forensic Medicine, Morgue Specialization Department between 2015 and 2020 have been studied. These cases were reviewed for autopsy information. Histopathology reports were also investigated. Three cases with cardiac rupture were considered as traumatic and two cases with inadequate autopsy information were not included in the study. The remaining 55 cases were reviewed. The age, gender, height, weight, body mass index, localization of rupture site, presence of pericarditis, presence of fibrin thrombus in coronary arteries, presence of stents or artificial valve, and a known history of hypertension, diabetes, and bypass were noted. Only cardiac wall ruptures due to myocardial infarction were included in the study. Rupture due to cardiopulmonary resuscitation and other types of traumatic causes were not included in the study.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) V21 2012 program was used for statistical analysis. While evaluating the study data, besides descriptive statistical methods (average, standard deviation, median, frequency, ratio, minimum, maximum), the Chi-squared test was used to compare qualitative data. Student's t-test was used to evaluate the difference between averages. Significance was evaluated at $p<0.05$ level.

RESULTS

Sixty autopsies of myocardial infarction with associated rupture were performed in the Council of Forensic Medicine, Morgue Specialization Department between 2015 and 2020. Three cases with traumatic cause and two cases with incomplete autopsy information were excluded from the study. Of the 55 cases included in the study, 45 (82%) were males and 10 (18%) were females. The age, height, weight, and body mass index of 53 cases are shown in Table 1. The age, height, weight, and body mass index according to gender are shown in Table 2. Two cases that did not have information about height and weight were not included in this analysis.

Most common sites of cardiac wall rupture were left ventricular lateral wall (n=16, 29%), left ventricular posterior wall (n=12, 22%), left ventricular anterior wall (n=10, 18%), left ventricular apex (n=7, 13%), interventricular septum (n=6, 11%), combined left ventricular anterior wall and septum (n=2, 4%), combined septum and left ventricular lateral wall (n=1, 2%), combined right ventricular posterior and lateral wall (n=1, 2%).

In our study, fibrin thrombus was detected in the lumens of the coronary arteries in 23 cases (42%) by histopathological examination (Fig. 1). Fibrin thrombus was found in 10 cases in the lumen of the left anterior descending coronary artery, 6 cases in the left circumflex coronary artery, and 7 cases in

Table 1. Age, height, weight, and body mass index of myocardial rupture cases

	Min.-max.	Mean±SD
Age (years)	40–94	63.1±12.2
Height (m)	1.5–1.8	1.7±8.8
Weight (kg)	45–117	77.3±13.7
BMI (kg/m^2)	17.6–35.4	27.4±4.1

BMI: Body mass index; Min: Minimum; Max: Maximum; SD: Standard deviation

Table 2. Age, height, weight, and body mass index of myocardial rupture cases according to gender

	Male	Female	p
Age (years)	61.9±10.6	68.1±17.9	<0.05
Height (m)	170.4±6.6	155±6.8	>0.05
Weight (kg)	79.5±13.9	66.8±5.6	>0.05
BMI (kg/m^2)	27.3±4.2	27.9±3.7	>0.05

BMI: Body mass index

the right coronary artery. In 10 cases where fibrin thrombus was detected in the lumen of the left anterior descending coronary artery, the ruptured area was observed in the anterior wall of the left ventricle, septum, and left ventricular apex in accordance with the perfusion zone of the left anterior descending coronary artery. In 6 cases where fibrin thrombus was detected in the lumen of the left circumflex coronary artery, the ruptured area was observed in the lateral wall of the left ventricle in 4 cases and the posterior wall of the left ventricle in 2 cases. In 7 cases, where fibrin thrombus was detected in the lumen of the right coronary artery, the ruptured area was observed in the posterior wall of the left ventricle in 3 cases, the posterior half of the septum in 3 cases, and the anterior wall of the left ventricle in 1 case.

Most of the cases did not have enough clinical information. Only 4 out of 55 cases had a history of known diabetes mellitus, 2 cases had a known hypertension history.

Twelve cases (22%) were histopathologically associated with pericarditis, while 43 (78%) were not (Fig. 2).

Two cases (4%) had the presence of a stent in the coronary arteries. No cases with a history of bypass surgery were reported.

Thirty-six (65%) cases had a history of cardiopulmonary resuscitation. Five (9%) cases did not have a history of cardiopulmonary resuscitation. The remaining 14 (25%) cases had no information about cardiopulmonary resuscitation.

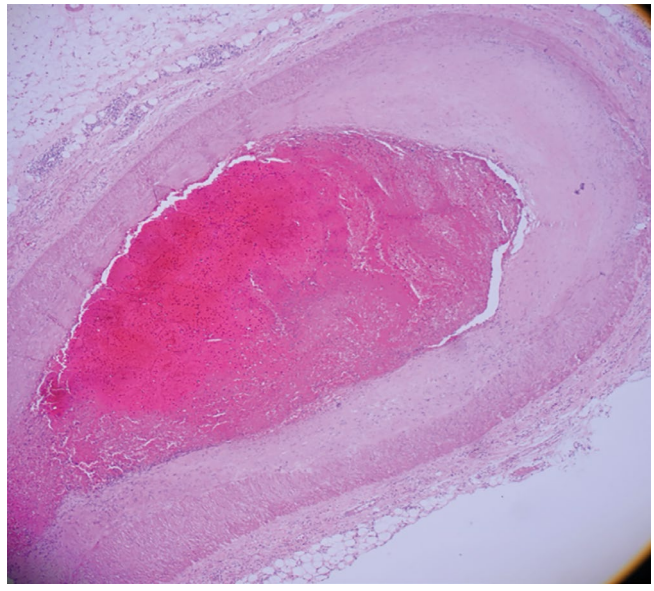

Figure 1. Fibrin thrombus in the lumen of coronary artery (H&E stain, 40×)

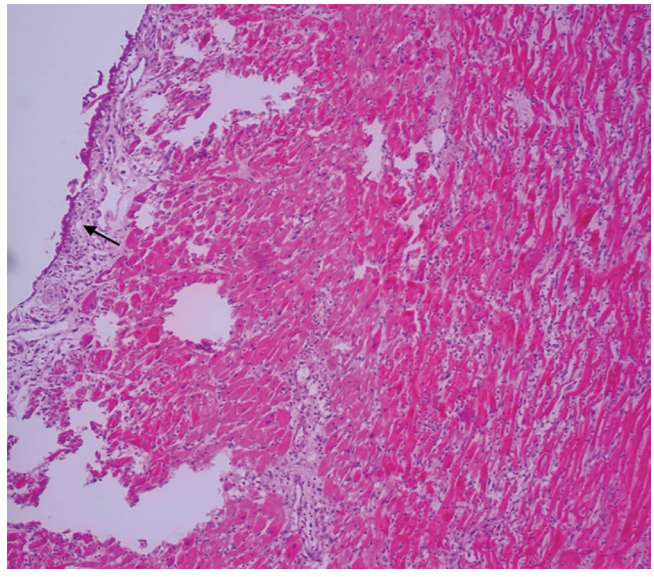

Figure 2. Fibrinous pericarditis at the epicardial surface (arrow) (H&E stain, 100×)

The evolution and dating of morphological changes in myocardial infarction are summarized in Table 3.

DISCUSSION

Studies in the pathogenesis of post-infarct cardiac rupture have indicated the basic roles of post-infarct myocardial inflammation, extracellular matrix (ECM) injury, and infarct

Table 3. Evolution and time course of myocardial infarction in the rupture

Time	Number (n)	Percentage
<24 h	19	34.5
1–3 days	9	16.4
3–7 days	17	30.9
7–10 days	10	18.2
Total	55	100

healing in the development of cardiac rupture.[12] Fibrillar collagen forms a three-dimensional network, providing tensile strength to the myocardium. It also preserves the alignment of adjoining myocytes. Infarcted myocardium surrounding the rupture site is found to be fragile and cause a reduction in tensile and mechanical strength of the infarct myocardium.[12] Myocardial infarction evokes intense inflammatory responses, which are essential for post-myocardial infarction healing and scar formation within the infarct myocardium. However, excessive inflammatory responses and ECM remodeling would contribute to adverse consequences, such as post-infarct cardiac rupture.[1,2] ECM composed of proteoglycans, collagen, fibronectin, elastin, fibrillin, and fibronectin is an organized multifunctional complex that contributes to the structural and functional integrity of the heart.[13] Following cardiomyocyte death and inflammation, cardiac healing starts. The formation of granulation tissue and the fibrotic healing process begins. Studies have shown that several ECM nonstructural molecules such as syndecans, biglycan, periostin, osteonectin, and osteopontin are critical in the fibrotic healing process and hence influence the risk of post-infarct cardiac rupture and ventricular remodeling.[12]

A 2–3 times higher incidence of rupture was found in male rats than in female rats. There was a significant gender difference in the risk of rupture.[12] More severe expansive ventricular remodeling was found in male rats after myocardial infarction than in female rats.[7,12] Also, less inflammatory cell accumulation in female rat hearts, intramural hemorrhage, lower levels of interleukin (IL-6 and IL-1B), reduced expression and activity of MMP-9, MMP-8, and metalloproteinase-1 tissue inhibitor (TIMP-1) were determined.[7,12] Decreased expression of TIMP-1 in female rats was consistent with higher levels of insoluble collagen content in females 4–7 days after myocardial infarction than in male rat myocardium. Thus, the gender gap in rupture risk can be explained, at least in part, by milder collagen destruction and an increase in fibrotic healing in female rat hearts.[7,12] Treatment of female rats with testosterone exacerbated cardiac inflammation and rupture incidence, while the administration of castration or estrogen to male rats reduced rupture incidence.[12,14] That knowledge was consistent with our study in which the male gender was significantly higher than the female (81.8% vs 18.2%). Although some studies indicate that rupture is more common in women, this information is still controversial and not consistent with our findings.[11,12]

Advanced age is recognized as a risk factor for heart rupture after infarction in humans.[12,15,16] It is believed that the cause of this increase is due to increased inflammation and damage to the ECM combined with aging.[12] Rich reported that elderly patients with acute myocardial infarction are more likely to experience heart failure, atrial fibrillation, cardiac rupture, and shock, all of which are associated with increased mortality.[17] In our study, the average age of the deceased was 63.1±12.2 years, which is in line with previous knowledge (Table 1). In addition, myocardial ruptures in women occur at a significantly older age than in men (61.9±10.6 vs 68.1±17.9). The gender difference of myocardial rupture is shown in Table 3.

Cardiac functional and hemodynamic conditions, such as heart rate and blood pressure, are considered risk factors affecting cardiac rupture after infarction.[12] In our study, due to difficulties in achieving past clinical information of autopsy cases, results that can make a clear assessment of hypertension and other risk factors were not achieved. That is also a limitation of our study.

While the size of infarction is known as an important predictor of hemodynamic complications and mortality after infarction, whether the size of infarction affects the risk of cardiac rupture remains unclear based on clinical studies.[12]

Hutchins et al.[18] and Becker et al.[19] reported that the anterior wall of the heart was the most vulnerable site of rupture. Oliva et al.[11] reported that the predilection of the sites of myocardial rupture was midlateral (32%), midanterior (26%), midinferior (18%), and other sites (24%).Gao et al.[12] reported anterior/lateral regions to be the most common rupture site. In our study, the most common site of rupture resulting from myocardial infarction was the left ventricular lateral wall (29%) in accordance with previous knowledge.

Evolution and dating of myocardial infarction at the site of rupture were recorded as less than 24 h, 1–3 days, 3–7 days, and 7–10 days according to the histopathologic findings (Table 3 and Fig. 3). Ventricular free wall rupture is divided into

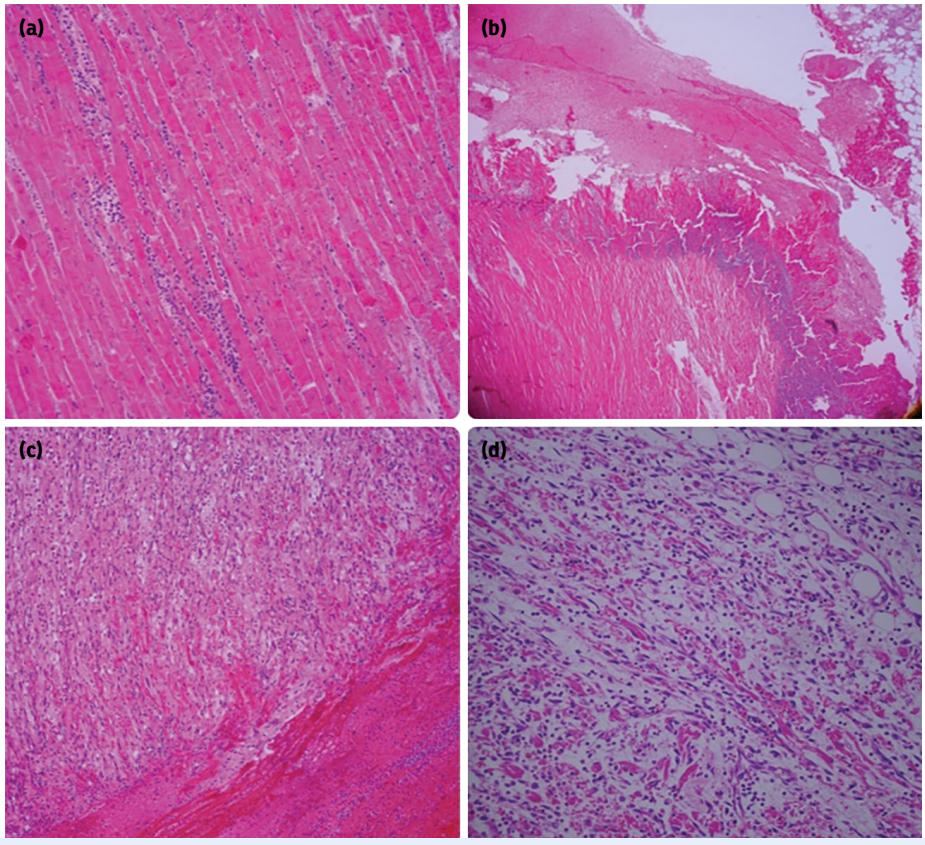

Figure 3. Microscopic evolution of myocardial infarction in rupture. **(a)** Less than 1-day-old myocardial infarction showing coagulative necrosis, loss of nuclei of cardiomyocytes, early neutrophilic infiltrate, and contraction band necrosis at the edge of infarct (H&E stain, 200×). **(b)** 1–3-day-old myocardial infarction showing coagulative necrosis, loss of nuclei of cardiomyocytes, and brisk neutrophilic infiltrate at the edge of infarct (H&E stain, 40×). **(c)** 3–7-day-old myocardial infarction showing disintegration of dead myofibers and phagocytosis of dead cells by macrophages at the edge of infarct (H&E stain, 100×). **(d)** 7–10-day-old myocardial infarction showing phagocytosis of dead cells and granulation tissue formation at the margins of infarct (H&E stain, 200×)

three according to Becker's classification: Type I and Type II (acute) ruptures occur 48 h after myocardial infarction. Type I has the form of a narrow slit, and Type II has the form of endocardial erosion. Type III rupture (subacute) occurs as a result of progressive thinning and expansion of the ventricular wall of the infarction within 3–10 days.[20–22] In our study, the myocardial rupture was observed as two peaks. The first and most frequent myocardial rupture time was the first 24 h of myocardial infarction (n=19, 34%). The second peak was between the third and seventh day of myocardial infarction (n=17, 31%). The myocardial rupture that develops after myocardial infarction occurs due to a softening of the myocardium over time, and a decrease in tensile strength before complete fibrosis develops during recovery.

Limitations

Failure to access the clinical history of autopsy cases is one of our main restrictions. Evaluating past clinical information together with autopsy and histopathological findings could allow us to assess associations with hypertension and diabetes and help us to achieve more descriptive results.

CONCLUSION

In our study, the myocardial rupture was detected most commonly in the first 24 h of myocardial infarction that is followed by between the third and the seventh day of myocardial infarction. The most common site of rupture caused by myocardial infarction was detected as the left ventricular lateral wall. Although some studies indicate that rupture is

more common in women, this is still controversial and not consistent with our findings in which men were significantly higher in number. The myocardial rupture was detected with older age. In addition, ruptures in women occur at a more advanced age than in men.

Disclosures

Acknowledgment: This study was carried out with the permission of the Council of Forensic Medicine Scientific Committee, and we thank them for their support.

Ethics Committee Approval: The study was approved by the Board of the Council of Forensic Medicine Scientific Ethics Committee (No: 21589509/855, Date: 21/06/2021).

Informed Consent: Is a retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions: Concept: T.D.; Design: T.D., A.B.; Supervision: T.D., A.B.; Funding: T.D.; Materials: T.D.; Data Collection or Processing: T.D., A.B.; Analysis or Interpretation: T.D., A.B.; Literature Search: T.D.; Writing: T.D.; Critical review: T.D.,A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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