



Frequency and severity of pericardial effusion after acute myocardial infarction

Abid Ullah Shah^{1*}, Muhammad Imran², Jafar Iqbal³, Adeel Ahmed Khalil⁴, Syed Arshad Ullah⁵, Waleed Ahmad⁶

¹Department of Cardiology, College of Medical Technology, Bacha Khan Medical College, Mardan, Pakistan

²Department of Cardiology, Institute of Paramedical Sciences, Khyber Medical University, Peshawar, Pakistan

^{3,4,5,6}Department of Cardiology, College of Medical Technology, Bacha Khan Medical College, Mardan, Pakistan

Key words: Acute myocardial infarction, Pericardial effusion, Echocardiography.

<http://dx.doi.org/10.12692/ijb/15.6.441-449>

Article published on December 29, 2019

Abstract

Pericardial Effusion (PE) is a complication after acute myocardial infarction (AMI), the objectives of this study was to determine the frequency and severity of PE after AMI and its association with other AMI complications. This cross sectional study was conducted in tertiary care hospital, Peshawar from March to August 2018. A total of 160 patients having AMI were included and data were collected through questionnaire after echocardiography test. PE was considered, if there is echo-free space in between visceral and parietal pericardium, when persist throughout cardiac cycle considered mild if <1cm, moderate 1-2cm and large > 2cm echo-free space. Both gender were included having age 25-85 years while patients with cardiomyopathies, heart failure, malignancy, TB and renal diseases were excluded from this study. All data was analyzed by SPSS-23. Out of 160 patients having AMI, 115 (71.9%) were male and 45 (28.1%) were female with mean age of 56.9±11.6 years. PE was found in 29 (18.1%) patients, mild and moderate PE was in 23 (14.4%) and 6 (3.8%) patients respectively. Majority of patients 82 (51%) were with acute anterior wall MI and no significant association ($p > 0.05$) were observed between location of AMI and PE. Other AMI complications such as mitral regurgitation, left ventricular dysfunction, LV clot, Ventricular aneurysm and ventricular septal rupture observed more in patients with PE and their association with PE proved statistically significant ($p < 0.05$). It is concluded that PE is a common complication after AMI and its complications are more in Patients with PE.

*Corresponding Author: Abid Ullah Shah ✉ abidullahshah22@gmail.com

Introduction

Acute myocardial infarction (AMI) commonly called “heart attack” is the rapid necrosis of myocardium due to sustained myocardial ischemia and is the leading complication of coronary artery disease (CAD) (Thygesen *et al.*, 2012), typical myocardial infarction (MI) is caused by dynamical atherothrombus, i.e. atherosclerosis and superimposed thrombus formation, in acute ST elevation myocardial infarction (STEMI) there is almost complete coronary arteries blockage and in Non-STEMI there is severely reduced coronary blood flow due to somewhat near complete coronary arteries occlusion (Davies, Woolf and Robertson, 1976; Davies and Thomas, 1985).

Pericardial effusion is an abnormal excess volume of pericardial fluid more than the upper reference range limit of normal (10-50ml) in between visceral and parietal pericardium (pericardial cavity) (Imazio and Adler, 2013). Pericardial effusion is a common and major complication of AMI, Irritant and hemodynamic factors like pericarditis, hydrostatic pressure, vascular permeability, osmotic pressure, pulmonary capillary wedge pressure contributes in development of PE (Sugiura *et al.*, 1990).

The frequency of pericardial effusion after AMI is different in different studies, e.g. in local studies (Pakistan) 32% in one study (Rehman *et al.*, 2010) and 27% in other study (Ali *et al.*, 2006) also show varies in severity but there is high variability among the frequency in different foreign studies 5.6% in one study (Wunderink, 1984) and 26% in other study (Pierard *et al.*, 1986).

The volume of pericardial effusion is also different with severity of myocardial infarction, that may be mild, moderate, severe and tamponade or life threatening and also the site of myocardial infarction has much influence in development of pericardial effusion, e.g. incidence of pericardial effusion is may influenced by location of AMI, study shows more associated with anterior wall MI than inferior, lateral, posterior or with other localized MI (Galve *et al.*,

1986).

There are other various post myocardial infarction complications, few major post-acute MI complications are mitral valve regurgitation, ventricular septal ruptures, impairment of left ventricular function, ventricular aneurysm, left ventricular thrombus, pericarditis, and others and nearly three of fourth patients suffers post MI complications, prompt diagnosis and timely management helps to prevent progressive deteriorations (Shah *et al.*, 2013; Riaz, Kaleem and Mughal, 2017).

Echocardiography is the ultrasound based investigation and is the choice of tool for the investigation of pericardial effusion and for assessment of grading its severity, i.e. mild, moderate, severe and diastolic collapse of cardiac chambers usually right ventricular or right atrium is seen in cardiac tamponade due to external compression by very large volume of pericardial effusion, also echocardiogram is an important diagnostic tool for investigation of other most of the post MI complications (Armstrong *et al.*, 1982; Parameswaran and Goldberg, 1983; OH, Seward and Tajik, 2006).

Studies shows huge range of difference in frequency, severity of pericardial effusion after AMI.

The current study was conducted to determine the frequency and severity of PE after AMI and also observed additionally the difference in frequency of other MI complications like mitral regurgitations (MR), ventricular septal rupture (VSR), ventricular aneurysm, impaired LV function and LV clots in patients with pericardial effusion and without pericardial effusion.

Material and methods

Study design, duration and setting

This cross sectional observational study was conducted in Cardiology Department of Northwest General Hospital and Research Center, Peshawar from March to August 2018.

Sample size, inclusion and exclusion criteria

A total of 160 patients with acute myocardial infarction were participated in present study. Patients of age 25-85 years with AMI irrespective of gender were included in current study.

On other side, patients with heart failure, cardiomyopathies, renal diseases, tuberculosis and malignancy were excluded from the study.

Study approval

The study was conducted after the approval from hospital concern authority.

Data collection procedure

Data regarding research was collected through convenience sampling from diagnosed admitted patients having acute myocardial infarction during hospital stay. Inform consent from research participants was the first step in data collection process and data were taken after patient's permission on volunteer basis and ensuring patients data confidentiality. All data was taken after proper echocardiography test under well experienced Echo Technologist after application of both 2D and M-mode, Doppler modalities and looking all the required views like parasternal long axis/short axis views, apical and subcostal views, pericardial effusion

was considered when echo-free space between parietal and visceral pericardium persists throughout the cardiac cycle and considered mild if the echo-free space was <1cm, moderate 1-2cm and large >2cm. Data regarding research was collected through questionnaire and all the required information related to research were included in the questionnaire.

Data analysis

All the variables like demographic, pericardial effusion, pericardial effusion severity, myocardial infarction and its major complications and others were entered and analyzed by using statistical package for social sciences (SPSS) version 23 software. Data was analyzed through descriptive statistics and any association was analyzed considering $p < 0.005$ as significant association.

Results

Total of 160 patients having acute myocardial infarction (AMI) were included in this study irrespective of gender, 115 (71.9%) were male and 45 (28.1%) female (Table 1).

The numbers of male were more than female patients with acute MI during this study duration.

Table 1. Sex of research participants (n=160).

Parameters	Frequency	Percent	Valid percent	Cumulative percent
Male	115	71.9	71.9	71.9
Female	45	28.1	28.1	100.0
Total	160	100.0	100.0	

The age of patients ranged from 25 to 85 years and participated minimum age was 26 years and maximum age was 85 years (mean \pm SD 56.86 ± 11.65 years). Age was further divide in to six groups, 6 (3.8%) patients were in 26-35 years age group and patients were lowest in this age group also, 17 (10.6%) in 36-45 years age group, in age group 46-55 there was 60 (37.5%) patients with AMI and was highest in this age group, 45 (28.1%) patients in 56-65 years group, 22 (13.8%) patients in 66-75 years, 10 (6.3%)

in 76-85 age group (Table 2), STEMI was present in 121 patients and NSTEMI was present in 39 patients (Table 2).

Pericardial effusion was found in 29 (18.1%) patients out of 160 patients having AMI and was absent in 131 (81.9%) patients. Pericardial effusion was mild in 23 (14.4%), moderate in 6 (3.8%) patients out of 29 (18.1) patients, and there were no patient with severe pericardial effusion or with tamponade (Table-

3). Acute anterior wall myocardial infarction was seen in majority 82 (51%) patients, inferior wall AMI was present in 39 (24.4%), lateral wall AMI in 8 (5.0%) patients, anterolateral wall AMI in 11 (6.9%), extensive anterior wall AMI in 8 (5.0%), inferolateral wall AMI was present in 12 (7.5%) patients respectively. Pericardial effusion was present in 18 cases of anterior wall AMI, 3 of inferior, 1 among

lateral and anterolateral, 4 among extensive anterior, 2 among inferolateral wall AMI patients respectively (Table 4).

No association observed between sites of AMI and pericardial effusion and it is proved statistically that there is no significant association between different sites of acute myocardial infarction and pericardial effusion ($p > 0.05$) (Table 4).

Table 2. Age groups of research participants and acute myocardial infarction type (n=160).

Parameters	Acute myocardial infarction type		Total AMI	Percentage
	STEMI	NSTEMI		
Age groups of research participants (Years)	26-35	4	6	3.8%
	36-45	13	17	10.6%
	46-55	52	60	37.5%
	56-65	32	45	28.1%
	66-75	14	22	13.8%
	76-85	6	10	6.3%
Total	121	39	160	100%

MR was present in 71 (44.4%) out of total 160 AMI patients, 23 patients were with both MR and pericardial effusion (PE) and in 48 patients with MR but without PE, LV clot was seen in 20 (12.5%) patients and was absent in 140 patients and there were 12 patients having PE and LV clots both, LV function was impaired in 96 (60%) patients and 64 (40%) patients were with normal LV function out of total 160 AMI patients, 26 patients were with both PE and impaired LV function, ventricular aneurysm was

observed in 4 (2.5%) patients and was absent in 156 patients, all patients with ventricular aneurysms were with PE as well, Ventricular septal rupture (VSR) was observed in only 3 (1.9%) patients and all these were with PE as well. A significant relationship observed between pericardial effusion with AMI complications like MR, LV clot, VSR, impaired LV function and ventricular aneurysm and statistically proved ($p < 0.05$) (Table 5).

Table 3. Frequency and severity of pericardial effusion (n=160).

Parameters	Frequency	Percent
Absent	131	81.9%
Mild	23	14.4%
Moderate	6	3.8%
Severe	0	0%
Tamponade	0	0%
Total	160	100.0%

Discussion

Pericardial effusion is common and usually early complication after acute myocardial infarction and its

frequency and severity is different from patients to patient with AMI, development of other post AMI complications like MR, LV clots, impaired LV

function, LV aneurysm, ventricular septal rupture (VSR) are also different in patients with PE and those without PE (Rehman *et al.*, 2010; Ali *et al.*, 2006; Wunderink, 1984).

The result of this study show pericardial effusion in 29 (18.1%) patients out of total 160 patients with acute myocardial infarction, PE was mild in 23 (14.4%), moderate in 6 (3.8%) patients and severe PE and tamponade was absent in patients during this study and other complications like MR, impaired LV function, LV aneurysm, VSR and LV clots were more in patients with pericardial effusion and their

significant associations established with pericardial effusion. Frequency of Pericardial effusion in this study was almost same with 16% result of another study (Kaplan *et al.*, 1985) but difference is they used M-mode only and same to this study Kaplan *et al* also found no association between age and location of infarction with pericardial effusion. Close to results of this study another study shows that mostly pericardial effusion is mild after AMI and Tamponade is very rare and also concludes 24-43% frequency of pericardial effusion after acute myocardial infarction (Gregor and Widimsky, 1999).

Table 4. Association of pericardial effusion and different sites of acute myocardial infarction (n=160).

Parameters		Acute myocardial infarction location						Total	p value
		Anterior	Inferior	Lateral	Antero lateral	Extensive anterior	Infero lateral		
Pericardial effusion	Yes	18	3	1	1	4	2	29	0.080
	No	64	36	7	10	4	10	131	
Total		82	39	8	11	8	12	160	

In this study both 2D and M-mode echocardiography modalities used unlike those of Wunderink (Wunderink, 1984), he carried out his study only with M mode echocardiography on 100 patients with acute myocardial infarction and found pericardial effusion in 5.6% of patients, results was very low than this study (18%) and this may be due to M-mode because it visualize only the selected region of heart, so localized PE may be missed with this technique. Wunderink also found that none of patients with pericarditis after AMI build PE.

Another study done in the Department of Cardiology and Medicine, Mayo Hospital, Lahore in 2006, in that study one hundred consecutive admitted patients presented within first day (24 hours) of first experience of ST elevation myocardial infarction were studied. After Echocardiographic examination and pericardial effusion was considered to be present when separation between parietal and visceral (epicardium) pericardium persisted throughout the cardiac cycle. Their results showed that among 100 patients who were studied 44 patients had acute

anterior MI and 38 patients were with inferior wall AMI, same higher patients with acute anterior MI in this study also found, result of that study shows pericardial effusion in 27 patients i.e. frequency of pericardial effusion was 27% that is higher than this study (18.1%) and in that study mild PE was found in 82 % patients, moderate PE was detected in 18%. Same to this study none of the patients developed large PE and tamponad. Other variables like gender, age and other CVS (cardiovascular) risk factors like diabetes were same in patients having PE and without PE (Ali *et al.*, 2006).

Another cross sectional study has done in department of cardiology, LRH (Lady Reading Hospital) Peshawar in 2007. Criteria for pericardial effusion (PE) was Echo-free space in between pericardial layers that persists throughout cardiac cycle. 200 adult patients with first acute myocardial infarction were included in the study. Frequency of pericardial effusion was higher than this study and was detected in 64 patients i.e. in 32% of patients. Nearly same to this study PE were seen more in patients with

anterior wall MI than others i.e. 16.5% in anterior myocardial infarction, 14% in inferior myocardial infarction and 15% in lateral myocardial infarction. Also other AMI complications like VSR (ventricular septal rupture) was found in 1 (0.5%) in patients having PE while no VSR recorded in patients without pericardial effusion and that study also concluded that left ventricular failure and in hospital mortality was also more in patients having pericardial effusion than those without PE after acute myocardial infarction (Rehman *et al.*, 2010). Another study done shows that incidence of pericardial effusions early in

AMI using two-dimensional echocardiography, 172 patients with an AMI were evaluated within 3 days of presentation. 30 (17%) patients had a pericardial effusion and was small in 29, moderate in one and no patient developed cardiac tamponade or required pericardiocentesis. Same to this study they found patients with pericardial effusion were with greater number of aneurysms 20% than without effusion aneurysms 6%, and concluded that PE was more associated with large MI and greater mortality than without pericardial effusion (Charlap *et al.*, 1989).

Table 5. Association of pericardial effusion with other acute myocardial Infarction complications (n=160).

Parameters	Pericardial effusion		Total	
	Yes	No		
Mitral regurgitation	Yes	23	48	71
	No	6	83	89
	Total	29	131	160
	p value	0.000		
LV Clot	Yes	12	8	20
	No	17	123	140
	Total	29	131	160
	p value	0.000		
Impaired LV function	Yes	26	70	96
	No	3	61	64
	Total	29	131	160
	p value	0.000		
LV aneurysm	Yes	4	0	4
	No	25	131	156
	Total	29	131	160
	p value	0.001		
Ventricular septal rupture	Yes	3	0	3
	No	26	131	157
	Total	29	131	160
	p value	0.005		

In this study out of 29 patients with PE, 23 with mild, 6 with moderate and no patient with severe or tamponade are observed, somewhat like study of Pierard *et al* (Pierard *et al.*, 1986), they applied 2D echocardiography in 66 consecutive patients with AMI and they observed PE in 17 (26%), small PE in 13 patients, moderate in 3 and only 1 patient with large

and signs of cardiac tamponade in only. Same to result of this study Pierard *et al* observation shows that pericardial effusion was not associated with age, sex and also complications like LV dysfunction, arrhythmias, and aneurysm were observed more in patients with PE than without PE. Pericardial effusion in AMI may occur due pericarditis or in the absence

of pericarditis, transmural infarction extends to pericardium and leads to pericarditis this lead to inflammation of visceral pericardium with loss of more fluid from myocardium to pericardial space through damaged epicardium and results in pericardial effusion, but in the absence of pericarditis hemodynamic factors like PCWP (pulmonary capillary wedge pressure) and advanced LV regional wall motion abnormalities leads to pericardial effusion (Sugiura *et al.*, 1990).

Results of this study also shows significant relationship between pericardial effusion and other AMI complications like MR, impaired LV function, VSR, ventricular aneurysm and these complications were more in patients with pericardial effusion than without pericardial effusion and likely these observations also reported in different studies (Pierard *et al.*, 1986; Sugiura *et al.*, 1990; Ali *et al.*, 2006; Rehman *et al.*, 2010) and some of them as well by Charlap *et al* (Charlap *et al.*, 1989).

Different studies shows that the presenting complaints of patient with pericardial effusions after AMI depends upon the volume and rapidity of accumulation pericardial effusion, mild or slowly developing large pericardial effusion may be without signs and symptoms but the chief complaints may be dyspnea, chest pain, cough, tachycardia, jugular venous distension, hypotension and muffled heart sound in cardiac tamponade (Ariyarah and Spodick, 2007; Sagrista-Sauleda, Merce and Soler-Soler, 2011; Stolz *et al.*, 2017).

Echocardiography is the choice of investigation tool for detection PE and grading its severity and helpful in management procedure like in pericardiocentesis. PE seen on echocardiography as echo-free space between visceral and parietal layers of serous pericardium that persist throughout cardiac cycle. Sensitivity of echocardiography to detect is very high even 20ml of fluid in pericardial space may be visualized, Horowitz *et al* observed that echo free space seen when there is more than 15ml of fluid in pericardial space. Echocardiography is used in

grading PE as mild if echo-free space less than 10mm, moderate 10-20mm, large >20mm and tamponade is seen as collapsing of cardiac chambers usually RV and RA (Horowitz *et al.*, 1974; Pate, Gardner and Norman, 1996; Lindenberger *et al.*, 2003; Pepi and Muratori, 2006; Sagrista-Sauleda, Merce and Soler-Soler, 2011; Saltzman *et al.*, 2012).

Conclusion

Pericardial effusion is common complication after acute myocardial infarction with varying degree of severity, most patients develops mild pericardial effusion, severe and tamponade or life threatening pericardial effusion after AMI are very rare.

There is significant association between pericardial effusion and other AMI complications like mitral regurgitation, impaired LV function, LV clots, ventricular aneurysm, ventricular septal rupture, hence possible chances of development of these complications increases in patients with pericardial effusion than without pericardial effusion after acute myocardial infarction.

Conflict of interest

Authors have no conflict of interest.

Acknowledgement

We are cordially thankful to Mr. Anees Muhammad, Lecturer, Department of Medical Laboratory Technology, College of Medical Technology, Bacha Khan Medical College, Mardan, for his guidance and valuable suggestions regarding this research project. We are also thankful to all staff of Cardiology Department of North West General Hospital and Research Center, Peshawar especially Mr. Shafi Ullah, Echo-Technologist, for his facilitation in data collection process.

References

Ali Z, Ahmad I, Sheikh S, Hameed S, Naveed T, Azhar M. 2006. Pericardial effusion in acute myocardial infarction: frequency and in-hospital course. *Annals of King Edward Medical University* **12(4)**, 563–565.

- Ariyarajah V, Spodick DH.** 2007. Cardiac Tamponade Revisited: A Postmortem Look at a Cautionary Case. *Texas Heart Institute Journal* 34, 347–351.
- Armstrong WF, Schilt BF, Helper DJ, Dillon JC, Feigenbaum H.** 1982. Diastolic collapse of the right ventricle with cardiac tamponade: An Echocardiographic study. *Circulation* 65, 1491–1496.
- Charlap S, Greengart S, Budzilowicz L, Gelbfish J, Hollander G, Shani J.** 1989. Pericardial Effusion Early in Acute Myocardial Infarction. *Clinical Cardiology* 12, 252–254.
- Davies MJ, Thomas AC.** 1985. Review Plaque fissuring—the cause of acute myocardial infarction, sudden ischaemic death, and crescendo angina. *British Heart Journal* 53, 363–373.
- Davies MJ, Woolf N, Robertson WB.** 1976. Pathology of acute myocardial infarction with particular reference to occlusive coronary thrombi. *British Heart Journal* 38, 659–664.
- Galve E, Garcia-Del-Castillo H, Evangelista A, Batlle J, Permanyer MG, Soler-Soler J.** 1986. Pericardial effusion in the course of myocardial infarction: incidence, natural history, and clinical relevance. *Circulation* 73, 294–299.
- Gregor P, Widimsky P.** 1999. Pericardial Effusion as a Consequence of Acute Myocardial Infarction. *Echocardiography* 16, 317–320.
- Horowitz MS, Schultz CS, Stinson EB, Harrison DC, Popp RL.** 1974. Sensitivity and specificity of echocardiographic diagnosis of pericardial effusion. *Circulation* 50, 239–247.
- Imazio M, Adler Y.** 2013. Management of pericardial effusion. *European Heart Journal* 34(16), 1186–1197.
<http://dx.doi.org/10.1093/eurheartj/ehs372>.
- Kaplan K, Davison R, Parker M, Przybylek J, Light A, Bresnahan D.** 1985. Frequency of pericardial effusion as determined by M-mode echocardiography in acute myocardial infarction. *The American Journal of Cardiology* 55(4), 335–337.
- Lindenberger M, Kjellberg M, Karlsson E, Wranne B.** 2003. Pericardiocentesis guided by 2-D echocardiography: the method of choice for treatment of pericardial effusion. *Journal of Internal Medicine* 253, 411–417.
- OH Jk, Seward JB, Tajik AJ.** 2006. Pericardial Disease. In *The Echo Manual*. 3rd edition. New Dehli: Wolter Kluwer, 289–310.
- Parameswaran R, Goldberg H.** 1983. Echocardiographic Quantitation of Pericardial Effusion. *Chest* 83, 767–770.
<http://dx.doi.org/10.1378/chest.83.5.767>.
- Pate JW, Gardner HC, Norman RS.** 1996. Diagnosis of Pericardial Effusion by Echocardiography. *Annals of Surgery* 165, 826–829.
- Pepi M, Muratori M.** 2006. Echocardiography in the diagnosis and management of pericardial disease. *Journal of Cardiovascular Medicine* 7, 533–544.
- Pierard LA, Albert A, Henrard L, Lempereur P, Sprynger M, Carlier J.** 1986. Incidence and significance of pericardial effusion in acute myocardial infarction as determined by two-dimensional echocardiography. *Journal of the American College of Cardiology* 8(3), 517–520.
[http://dx.doi.org/10.1016/S0735-1097\(86\)80177-2](http://dx.doi.org/10.1016/S0735-1097(86)80177-2).
- Rehman H, Khan SB, Hadi A, Nawaz T, Shah ST, Ullah H.** 2010. Frequency of pericardial effusion in patients with first myocardial infarction and its effects on in-hospital morbidity and mortality. *Journal of Ayub Medical College Abbottabad* 22(2), 184–186.
- Riaz A, Kaleem M, Mughal S.** 2017. Frequency of

Complications of anterior wall myocardial infarction. Pak Heart Journal **50(03)**, 190–193.

Sagrsta-Sauleda J, Merce AS, Soler-Soler J. 2011. Diagnosis and management of pericardial effusion. World Journal of Cardiology **3(5)**, 135–143.

Saltzman AJ, Paz YE, Rene AG, Green P, Hassanin A, Argenziano MG. 2012. Comparison of surgical pericardial drainage with percutaneous catheter drainage for pericardial effusion. Journal of Invasive Cardiology **24(11)**, 590–593.

Shah SFA, Hadi A, Faheem M, Ikramullah, Iqbal MA, Gul AM. 2013. Frequency of mechanical complications in patients with acute myocardial infarction. Pak Heart Journal **46(02)**, 86–90.

Stolz L, Valenzuela J, Situ-LaCasse E, Stolz U, Hawbaker N, Thompson M. 2017. Clinical and

historical features of emergency department patients with pericardial effusions. World Journal of Emergency Medicine **8(1)**, 29–33.

<http://dx.doi.org/10.5847/wjem.j.1920>.

Sugiura T, Iwasaka T, Takayama Y, Matsutani M, Hasegawa T, Takashi N. 1990. Factors Associated With Pericardial Effusion in Acute Q Wave Myocardial Infarction. Circulation **81**, 477–481.

Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Alpert JS, White HD. 2012. Third universal definition of myocardial infarction. European Heart Journal **33**, 2551–2567.

<http://dx.doi.org/10.1093/eurheartj/ehs184>.

Wunderink RG. 1984. Incidence of Pericardial Effusions in Acute Myocardial Infarctions. Chest **85(4)**, 494–496.

<http://dx.doi.org/10.1378/chest.85.4.494>