

# ASSESSMENT OF CARDIAC CONTRACTILITY IN PEDIATRIC PATIENTS WITH PNEUMONIA USING ECHOCARDIOGRAPHY AND CREATINE KINASE-MB

By

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## ABSTRACT

**Introduction:** Community acquired pneumonia (CAP) is the most common cause of infant mortality worldwide, and one of the most common serious pediatric infectious diseases in developed countries. Recent studies documented a frequent association between CAP and the occurrence of acute cardiac complications.

**Aim of the work:** The aim of this study is to assess myocardial affection in children hospitalized with community acquired pneumonia. Markers used are assessing blood levels of CK-MB and imaging with Echocardiography.

**Methods:** This cross sectional case-control study. It was conducted at Al-Hussein hospital Al-Azhar University from July 2020 to February 2021, on 50 cases. 28 were males and 22 were females. Patients' age's ranges from 6 months to less than 5 years admitted with respiratory distress and diagnosed as community acquired pneumonia. The control group consisted of 50 matched healthy children of the same gender and age.

**Results:** CK-MB level showed significant increase in cases compared to controls ( $10.8 \pm 2.1$  ng/ml) versus ( $2.7 \pm 0.08$  ng/ml) ( $P$ -value 0.003), Echocardiography in cases with CAP showed significant diastolic dysfunction as compared to control group. Oxygen saturation showed significant negative correlation with severity of diastolic dysfunction as demonstrated by Septal and Lateral  $E/e'$  ratio.

( $E$  = Peak early mitral inflow velocity and  $e'$  = Tissue Doppler velocity of mitral annulus).

**Conclusion:** The current study showed a significant statistical difference between cases and controls as regard CK-MB levels and the ability of Echocardiographic imaging for detection of myocardial contractility affection in cases of CAP and its severity. It also points towards the ability of pulse oximetry and CK-MB to predict cardiovascular outcome in CAP cases.

**Key words:** Conventional echo Doppler, Creatine kinase-MB, myocardial affection, acute pneumonia, pediatrics.

## INTRODUCTION

Community acquired pneumonia (CAP) is the most common cause of infant mortality worldwide, and one of the most common serious pediatric infectious diseases in developed countries (Han et al., 2018).

Recent studies documented a frequent association between CAP and the occurrence of acute cardiac complications such as heart failure (HF), atrial fibrillation (AF), and myocardial infarction (MI) (Violi, Francesco, et al., 2017).

Moreover, the occurrence of these complications in patients with CAP has been associated with increased short- and long-term mortality (Cangemi et al., 2015).

Echocardiography has become the most important non-invasive technique for the diagnosis and follow-up of heart disease in children (Nimdet and Techakehakij, 2020).

Many biomarkers are used in clinical practice to identify myocardial injury; CK-MB and troponin I (cTnI) are the most commonly used biomarkers (Hassan et al., 2014).

CK-MB is one of the three isoforms of the enzyme creatine kinase (CK), CK is not specific to AMI. Therefore, the CK test has been gradually abandoned and replaced by CK-MB because it is more specific in the heart muscle (Nimdet and Techakehakij, 2020).

## AIM OF THE WORK

This study aimed to assess myocardial affection in children hospitalized with community acquired pneumonia by assessing blood levels of CK-MB with the help of echocardiography.

## Ethical Consideration:

1. A written informed consent was obtained from parents or the legal guardians before the study.
2. An approval by the local ethical committee was obtained before the study.
3. The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.
4. All the data of the patients and results of the study are confidential & the patients have the right to keep it.

5. The patient has the right to withdraw from the study at any time.

### **Financial Disclosure / Funding:**

The authors received no financial support for the research, authorship and/or publications of this article.

### **PATIENTS AND MATERIALS**

This case-control cross-sectional study was conducted at Al-Hussein university hospital, Faculty of Medicine, Al-Azhar University during the period from July 2020 to February 2021, on 50 cases 28 were males and 22 were females and 50 matched healthy children of the same gender and age. Patients' ages ranged from 6 months to less than 5 years.

#### **I. Patients:**

##### **Inclusion criteria:**

All cases are aged from 6 months to less than 5 years (of both sexes) who were diagnosed as having community acquired pneumonia (CAP) as defined clinically, laboratory and radiologically by both British Thoracic Society (BTS) and the Infectious Disease Society of America (IDSA).

##### **Exclusion criteria:**

- Patients with chronic diseases e.g: chronic chest diseases,

hepatic, renal diseases or congenital heart diseases.

- Patients with hospital acquired pneumonia.
- Children suspected to have COVID-19 infection according to Egyptian protocol for management of COVID-19 in pediatrics.

#### **II. Methods:**

**All the studied cases were subjected to the following:**

##### **A. History:**

- Personal history: name, age, sex, residence, socioeconomic status, parent education, contact with animal or source of pollution.
- Past history of recurrent chest infection or hospital admission.
- Family history, vaccination history, developmental and dietetic history,

##### **B. Examination:**

- The vital signs including blood pressure, heart rate, respiratory rate, SPO<sub>2</sub> and body temperature were recorded.
- Anthropometric measurements (height & weight).
- General examination: Head & neck, abdomen, back, UL and LL.

- Local examination: Chest and cardiac examination; by inspection, percussion, auscultation of both heart and chest.

### C. Investigations:

- Complete blood count by Sysmex x5-800 (Sysmex Corporation, Japan).
- Quantitative assessment of C-reactive protein (CRP) by latex agglutination test (TURBOX plus Orion Diagnostica, Finland).
- Arterial blood gases by Cobas b 221 system, USA.
- Radiological imaging: Chest x ray to all patients while CT chest was done only when indicated.
- CK-MB analysis for cases and control groups:

### Method of assay:

- The test was done by sandwich principle on the e-411 cobas instrument according to the manufacturer instructions (05957648190) (Roche Diagnostics GmbH, Sandhofer 116, D-68305 Mannheim www.roche.com).
- For quality control, the preci control cardiac II was used.
- The reagents were stored at 2-8° c till the assay date.

### Sample collection:

Whole blood samples were collected on red capped vacutainer tubes, centrifuged at 3000 rpm for 15 min, serum is separated and freezed at 20°c in aliquots till the assay date.

### Echocardiography:

Echo-Doppler examination was performed for all cases in a supine or left lateral position using Philips EPIQ 7C (multifrequency transducer) according to the age of patient, having tissue velocity imaging capabilities.

#### a. Conventional Echo-Doppler measures:

The examination was performed by pediatric cardiologists who are experts in echocardiography. The examination was consisted of M-mode, 2-D, pulsed, continuous wave and color Doppler blood flow velocity measurements of the heart valves.

#### For M-mode the following measurements were done:

1. In the parasternal long-axis view, at the level of the tips of the mitral valve leaflets: IVSD, IVSS, LVDD, LVDS, LVPWD, LVPWS, FS, EF were measured.

2. In the parasternal long-axis view, at the level of the aorta and left atrium, LA & aortic diameter were measured.

PW Doppler was used for each cardiac valve separately. Colour flow mapping was used for helping alignment of Doppler beam, grading of valve regurge. CW Doppler over tricuspid regurge was used for measurement of pulmonary pressure.

(Tei index) was calculated and is defined as the sum of isovolumic contraction time (ICT) and isovolumic relaxation time (IRT) divided by ventricular ejection time (ET).

**b. Tissue velocity imaging (TVI) measures**

1. Pulsed Tissue velocity imaging (TVI) measures included systolic myocardial velocities at the basal segments of the lateral LV wall, septal wall and RV free walls (LV-Sm, septal-Sm and RV-Sm, respectively), early and late diastolic myocardial velocities and their ratio (Em, Am and Em/Am,

respectively) of the same basal segments.

2. Calculation of global myocardial performance index (Tei index) by pulsed tissue velocity imaging.

**Statistical Methods:**

Data were analyzed using MedCalc<sup>®</sup> version 18.2.1 (MedCalc<sup>®</sup> Software bvba, Ostend, Belgium).

Continuous numerical variables were presented as mean ± SD and inter-group differences were compared using the unpaired t test for two-group comparisons or one-way analysis of variance (ANOVA) for multiple-group comparisons.

Categorical variables were presented as ratio or number and percentage and differences were compared using Fisher’s exact test.

Correlations were tested using the Pearson product-moment correlation. The correlation coefficient (Pearson r) is interpreted as follows:

**Table (1): Interpretation of correlation coefficient**

Correlation coefficient	Strength of correlation
<0.2	Very weak
0.2 – 0.39	Weak
0.4 – 0.59	Moderate
0.6 – 0.79	Strong
0.8 – 1.0	Very strong

P-values <0.05 were considered statistically significant.

## RESULTS

**Table (2): Comparison of The Demographic Characteristics in Cases and Controls**

Variable	Acute pneumonia (n=50)	Control (n=50)	p-value*
Age (months)	12.3 ± 2.3	14.8 ± 3.1	0.34
Residence			
Urban n (%)	33 (66%)	37 (74%)	0.28
Rural n (%)	17 (34%)	13 (26%)	
Gender			
Males n (%)	28 (56%)	31 (62%)	1.000
Females n (%)	22 (44%)	19 (38%)	

\*Unpaired t-test unless otherwise Indicated. #Fisher's exact test.

This table shows insignificant difference between cases and controls as regard demographic data.

**Table (3): Clinical and Laboratory Characteristics of Patient Group (N=50)**

Variable	Mean ± SD / n (%)
<b>PRESS score</b>	
Mild	11 (22 %)
Moderate	23 (46 %)
Severe	16 (32 %)
<b>ABG</b>	
PH	7.43 ± 0.17
SPO <sub>2</sub> (%)	89 % ± 3.4
PaCO <sub>2</sub> (mmHg)	31.2 ± 7.7
HCO <sub>3</sub> (mmol/l)	31.2 ± 7.7
<b>CBC</b>	
TLC (x10 <sup>3</sup> /ml)	15.6 ± 3.7
Neutrophils (%)	81 % ± 4.3
Lymphocytes (%)	21 % ± 3.9
Hemoglobin (g/dl)	9.2 ± 2.1
Platelets (x10 <sup>3</sup> /ml)	183 ± 42
<b>CRP (mg/l)</b>	41 ± 8.3

\*PRESS score: pediatric respiratory severity score.

This table shows that the majority of cases had moderate respiratory distress (46% had moderate PRESS score. It also shows that there's mild

hypoxemia (SPO<sub>2</sub> level = 89% ± 3.4). There's also marked neutrophilia (81% ± 4.3) and elevated CRP level (41 ± 8.3).

**Table (4): Outcome and Survival of Patient Group N=50**

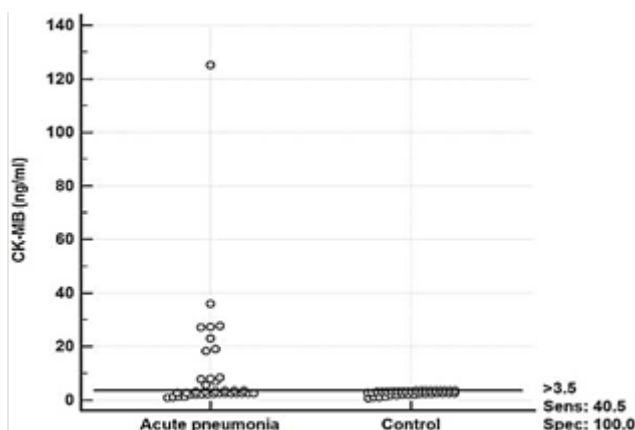
<b>Outcome</b>	
Cured n(%)	40 (80 %)
Complicated n(%)	9 (18 %)
Sepsis n(%)	7 (14%)
Pleural effusion n(%)	2 (4%)
Died n(%)	1 (2 %)
<b>Overall survival</b>	
Survived n(%)	49 (98 %)
Died n(%)	1 (2 %)

This table shows that only 1 were complicated with all case died out of 50 and 9 cases survival rate = 98%.

**Table 5: Comparison of CK-MB Levels in Cases and Controls**

Variable	Acute pneumonia (n=50)		Control (n=50)		p-value*
	Mean	SD	Mean	SD	
CK-MB (ng/ml)	10.8	2.1	2.7	0.08	0.003

Unpaired t-test. Normal reference range of CK-MB = (0 - 4.9 ng/ml)  
 CKMB showed significant rise in cases compared to controls.



**Figure (1): Interactive dot diagram showing CK-MB levels in cases and controls.**

**Table (5)** and **Figure (1)** represents an interactive dot diagram demonstrating that CK-MB can discriminate between cases and controls with high

specificity reaching up to 100%, however it cannot be used as a screening tool due to its low sensitivity 40%.

**Table (6): Comparison of Echocardiographic Parameters in Cases and Controls**

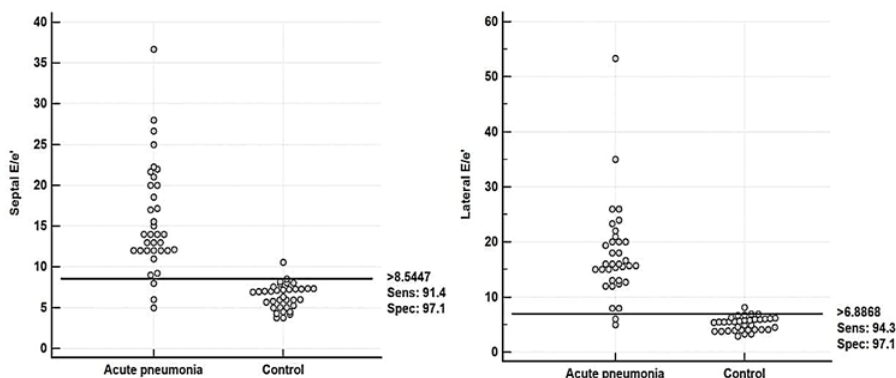
Variable	Acute pneumonia (n=50)		Control (n=50)		p-value*
	Mean	SD	Mean	SD	
LVEDVI (ml/m <sup>2</sup> )	73.7	3.5	71.5	1.9	0.06
Septal E' (cm/s)	8.4	1.2	14.3	1.7	<0.0001
Septal A' (cm/s)	7.6	2.6	7.4	1.7	0.693
Lateral E' (cm/s)	7.7	1.3	17.7	1.3	<0.0001
Lateral A' (cm/s)	8.2	0.4	7.3	0.4	0.132
Mitral E (m/s)	1.2	0.2	0.9	0.2	<0.0001
Septal E/e'	15.8	2.6	6.4	1.1	<0.0001
Lateral E/e'	17.7	1.2	5.2	1.1	<0.0001
FS (%)	38.8	5.3	37.3	3.3	0.167
EF (%)	75.2	10.3	72.9	5.1	0.07

Unpaired t-test.

LVEDVI = left ventricle end diastolic volume index, E= Peak early mitral inflow velocity, E'= peak mitral annular velocity during early diastole; normal septal ≥8cm/s, lateral ≥10cm/s, while normal E/e' <8 (septal, lateral, or average of both), A'= peak annular velocity during late diastole, EF= ejection fraction, FS= fraction shortening.

**Table 6** shows that only tissue Doppler derived parameters namely septal E/e' ratio and lateral E/e' ratio among

other echocardiographic parameters were able to differentiate cases from controls.



**Figure (2): 2 Interactive dot diagram showing Septal and Lateral E/e' in cases and controls**

More over Septal E/e' and lateral E/e' are not only significantly different between the 2 study groups by **figure (2)** (2 interactive dot diagrams), show a

high sensitivity and specificity for the aforementioned parameters for discrimination between the study groups.



**Table (7): Correlation between CK-MB Level and Echocardiographic Measures with The Outcome of Pneumonia**

Variable	Complicated or died			Cured			Difference	95% CI	p-value*
	N	Mean	SD	N	Mean	SD			
CK-MB (ng/ml)	10	14.3	6.7	40	5.1	26.3	-9.2	-5.4to 23.9	0.008
LVEDVI (ml/m <sup>2</sup> )	10	78.3	3.9	40	74.0	4.3	-0.8	-1.8 to 3.3	0.065
Septal E' (cm/s)	10	9.1	3.8	40	8.0	2.9	-1.0	-3.4 to 1.3	0.003
Septal A' (cm/s)	10	7.4	2.5	40	6.7	2.7	-0.7	-1.7 to 2.1	0.378
Lateral E' (cm/s)	10	8.8	4.0	40	7.2	2.9	-1	-4.0 to 0.7	0.027
Lateral A' (cm/s)	10	8.9	2.2	40	7.8	2.5	-1.1	-2.8 to 0.7	0.221
Mitral E (m/s)	10	1.2	0.3	40	0.7	0.2	-0.5	-0.2 to 0.2	0.043
Septal E/e'	10	16.8	4.8	40	13.7	7.3	-2.9	-1.8 to 7.8	0.003
Lateral E/e'	10	18.4	5.8	40	15.9	9.7	-2.5	-2.7 to 9.7	0.002
FS (%)	10	38.3	5.1	40	43	5.4	4.7	-6.1 to 1.6	0.047
EF (%)	10	73.8	9.7	40	77.9	10.6	4.1	-11.6 to 3.3	0.049

\*Unpaired t test.

**Table (7)** shows that both CK-MB and relevant echocardiographic parameters (septal and lateral E/e') can be used as predictive values for the

outcome of Pneumonia this evidenced by significantly increasing level of CK-MB in complicated cases.

**Table (8): Correlation between the Spo2, CK-MB and Echocardiographic Parameters in Cases**

Variable	SpO <sub>2</sub>	
	Pearson r	p-value
CK-MB	-0.110	0.515
LVEDVI	-0.090	0.607
Septal E'	0.538**	0.001
Septal A'	0.321	0.060
Lateral E'	0.731**	<0.001
Lateral A'	0.398*	0.018
Mitral E	-0.420*	0.012
Septal E/e'	-0.790**	<0.001
Lateral E/e'	-0.775**	<0.001
FS	0.037	0.832
EF	0.025	0.886

**Table (8)** demonstrates that there's positive correlation between Spo<sub>2</sub> level and severity

of diastolic dysfunction as demonstrated by Septal and Lateral E/e'.

**Table (9): Correlation between Echocardiographic Parameters and The PRESS Score**

Echocardiographic parameter	Correlation coefficient	PRESS score
LVEDVI	Spearman rho	0.088
	p-value	0.613
Septal E'	Spearman rho	0.009
	p-value	0.018
Septal A'	Spearman rho	0.278
	p-value	0.105
Lateral E'	Spearman rho	0.017
	p-value	0.032
Lateral A'	Spearman rho	0.008
	p-value	0.966
Mitral E	Spearman rho	0.018
	p-value	0.024
Septal E/e'	Spearman rho	0.019
	p-value	0.031
Lateral E/e'	Spearman rho	0.005
	p-value	0.037
FS	Spearman rho	0.064
	p-value	0.717
EF	Spearman rho	-0.071
	p-value	0.687

**Table (9)** shows that impairment of echocardiographic parameters

correlate with severity of Pneumonia which assessed by PRESS score.

### **DISCUSSION**

This is a case-control cross-sectional study. The main goal of our study is to answer whether community acquired pneumonia is affecting myocardium or not. And which forms of myocardial involvement predominate and if the severity of myocardial involvement correlates with the severity of pneumonia.

The Echocardiographic parameters, were made for identifying patients with asymptomatic cardiac dysfunction may allow the implementation of non-pharmacological or pharmacological interventions.

In our study we assessed systolic function using M-Mode echocardiography we found that FS and EF proved no statistically

significant difference between cases and controls.

Several reasons may explain such finding, but the most important of which is the lack of Sensitivity and specificity of M-mode derived parameters this coincidence with **Chengode. (2016)** who stated that M-mode do not represent global LV shortening in the presence of regional wall motion abnormalities (RWMA), overestimation of overall LV function is impossible because basal segments contract adequately even in a significant LV systolic dysfunction. Meanwhile, the parameters of diastolic Function, were measured in our patients using conventional Doppler derived septal E/e' ratio (**Nagueh et al., 2016**).

In our study, Septal E/e' and Lateral E/e' parameters showed statistically significant difference between cases and controls. This denotes early diastolic dysfunction in pneumonia cases. This goes in agreement with **Kalra et al. (2013)** study which proved that diastolic dysfunction in the context of pneumonia precedes systolic impairment. Nevertheless, hypoxia could correlate very well with the severity of diastolic dysfunction.

In our study, we found that there is a statistically significant

increase between cases and controls regarding CK-MB level. The result of our study is in concordance with previous study by **Ferrari et al. (2012)**, who showed that CK-MB level was higher in ordinary pneumonia cases and severe pneumonia cases than control.

CK-MB has been useful for screening myocardial affection in cases with pneumonia and thus CK-MB levels can correlate with the severity of pneumonia.

CK-MB could help in predicting the outcome of CAP. This is in concordance with study by **Han et al. (2018)**, who reported that the higher the levels of myocardial enzymes in children with severe pneumonia, the more serious the condition of myocardial damages.

## **CONCLUSION**

Our study concluded that, Conventional Doppler echocardiography in cases with CAP showed significant diastolic dysfunction compared to control group. In children with community acquired pneumonia, serum. CK-MB is significantly higher than control group. Also, Oxygen saturation show significant correlation with echocardiography parameters. The outcome and morbidity of CAP in

our study cases were good (1 case died due to proper management).

### **RECOMMENDATION**

- The use of Routine Tissue Doppler is useful in early detection of myocardial changes in community acquired pneumonia patients.
- Cardiac enzyme CK-MB assessment may have diagnostic and prognostic of cardiac affection in children with community acquired pneumonia.
- Regular assessment and follow up of Oxygen saturation by pulse oxymeter is an important test in community acquired pneumonia patients.
- Diagnosis and management of cardiovascular complications in these patients may improve overall outcome in childhood CAP.
- Further studies are needed to elucidate the spectrum of cardiovascular changes and their clinical and therapeutic implications in cases with CAP.

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# تقييم مدى تأثير انقباض عضلة القلب في الأطفال المصابين بالالتهاب الرئوي عن طريق عمل موجات صوتية على القلب وقياس نسبة الكرياتين كينيز إم بي

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قسم طب الأطفال\* والباثولوجيا الاكلينيكية\*\* كلية الطب جامعة الأزهر بنين القاهرة  
الالتهاب الرئوي هو عملية لالتهاب الحويصلات الهوائية والمساحات الهوائية الطرفية والذي عادة ما يكون نتيجة للغزو من جانب عوامل معدية كالبكتريا والفيروسات وغيرها من الميكروبات التي يتم ادخالها الي الرئتين عن طريق الاستنشاق او الانتشار.

الالتهاب الرئوي من أهم أسباب الوفاة في مرحلة الطفولة، لاسيما في مرحلة الرضاعة من سن شهر حتى سنتين. اذ انه لا يمكن التفكير في الجهاز التنفسي والقلب والأوعية الدموية بشكل مستقل. لذلك من المهم الكشف عن التغييرات في القلب والأوعية الدموية أثناء الالتهاب الرئوي.

ارتفاع إنزيم الكرياتين كينيز إم.بي يحدث خاصة نتيجة تلف في عضلة القلب. وقد يكون العلامة الوحيدة على التهاب العضلة القلبية.

الموجات فوق صوتية على القلب أصبح اهم وسيلة  
لتشخيص ومتابعة أمراض القلب في الأطفال.

هذه الدراسة تمت في مستشفى الحسين جامعة الأزهر  
فرع القاهرة على 50 حالة من الأطفال الذين أصيبوا بالتهاب  
رئوي حاد وتم حجزهم في الأقسام الداخلية والرعاية المركزة  
وعلى 50 طفل طبيعي. هؤلاء الأطفال تتراوح أعمارهم ما بين  
سنة أشهر وخمس سنوات.

الهدف من هذه الرسالة هو تقييم التغيرات التي تحدث  
في القلب نتيجة الالتهاب الرئوي الحاد عن طريق وسائل غير  
اقتحاميه في الأطفال.

تم استخدام الموجات فوق صوتية على القلب (دوبلر)  
وإنزيم الكرياتين كينيز إم.بي لكي نحدد التغيرات في عضلة  
القلب.

**توصلت هذه الدراسة الي الآتي:**

- انزيم الكرياتين كينيز في الأطفال المصابين بالتهاب رئوي  
حاد أعلى من مجموعة الاطفال الطبيعية.
- دوبلر الأنسجة في الأطفال المصابين بالتهاب رئوي حاد  
أظهر حدوث عجز انبساطي في عضلة القلب مقارنة  
بمجموعة الاطفال الطبيعية.
- درجة تشبع الاكسجين لها ارتباطات مباشرة مع درجة تأثر  
القلب باستخدام تخطيط صدي القلب.
- هناك ارتباط بين درجة الالتهاب الرئوي ونتائجه مع انزيم  
الكرياتين كينيز إم.بي والتغيرات في تخطيط صدي القلب.