The prognostic value of Tei index in acute myocardial infarction: A systematic review

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Short Title: The prognostic value of Tei index in AMI

Keywords: Echocardiography, Tei index, myocardial performance index, myocardial infarction, prognosis

Word count: 4588
Abstract

**Background:** Echocardiographic evaluation of left ventricular ejection fraction (LVEF) is used in the risk stratification of patients with an acute myocardial infarction (AMI). However, the prognostic value of the Tei index, an alternative measure of global cardiac function, in AMI patients is not well established.

**Methods:** We conducted a systematic review, using MEDLINE and EMBASE, to evaluate the prognostic value of the Tei index in predicting adverse outcomes in patients presenting with AMI. The data was collected and narratively synthesized.

**Results:** A total of 16 studies were including in this review with 2886 participants (mean age was 60 years from 14 studies, proportion of male patients 69.8% from 14 studies). Patient follow-up duration ranged from during the AMI hospitalisation stay to 57.8 months. Tei index showed a significant association with heart failure episodes, re-infarction, death and left ventricular thrombus formation in 14 out of the 16 studies. However, in one of these studies, Tei index was only significantly predictive of cardiac events in patients where LVEF was <40%. In two further studies, Tei index was not associated with predicting adverse outcomes once LVEF, left ventricular end systolic volume index and left ventricular early filling time was taken into consideration. In the two remaining studies, there was no prognostic value of Tei index in relation to patient outcomes.

**Conclusions:** Tei index may be an important prognostic marker in AMI patients however more studies are needed to better understand when it should be used routinely within clinical practice.
Introduction

First described in 1995, Tei index, also known as myocardial performance index, is a ratio of systolic and diastolic time intervals which can be easily obtained from Doppler echocardiography. This timing ratio, characterised by the sum of the isovolumetric contraction time and isovolumetric relaxation time divided by the overall ejection time, has been well validated in the assessment of overall global myocardial performance in both adult and paediatric populations. Although Tei index is not a frequently used measurement in assessing cardiac function in current clinical practice, there is evidence to suggest that the Tei index is a simple, reliable and reproducible measurement in patients with congestive heart failure, congenital heart disease and cardiac rejection post transplantation. Tei index has also been shown to have prognostic value in patients with cardiac amyloidosis and dilated cardiomyopathy.

An acute myocardial infarction (AMI) is a leading cause of morbidity and mortality worldwide with known complications including congestive heart failure, functional and structural myocardial abnormalities, re-infarction and death. In the setting of an AMI, echocardiography is a well-established risk stratification tool. Consequently, echocardiographic assessment in the early post AMI stage forms part of national and international guidelines. An important echocardiographic measurement for post AMI patients is the assessment of left ventricular systolic function via left ventricular ejection fraction (LVEF) which is well associated with short-term and long-term outcomes. However, it is well recognised that systolic and diastolic function are tightly connected at a cellular, myocardial and hemodynamic level. As such, Tei index, which considers both contraction and relaxation timing intervals, may provide important prognostic information in patients presenting with AMI which may go unmissed with the isolated evaluation of LVEF. Furthermore, the Tei index is less affected by image quality compared to LVEF and GLS which makes the index an attractive parameter for the assessment of global left ventricular function.

Studies in the literature evaluating the prognostic value Tei index after AMI are inconsistent with studies reporting an association between a greater Tei index and adverse events. Whilst other studies either conclude there to be no association or, that Tei index offer no additional benefit over the more routinely used LVEF measurement. In view of the importance of understanding the prognostic value of the Tei index in AMI patients and the inconsistencies reported, we conducted a systematic review of the literature to evaluate what is currently known.
Methods

We conducted a systematic review to evaluate the current literature on the prognostic value of Tei index in patients presenting with an AMI. Tei index was defined as per Figure 1. Study inclusion criteria included: retrospective cohort studies, prospective cohort studies and matched control studies. Excluded criteria consisted of conference abstracts, animal studies, case studies, case series, studies using bare metal stents used as part of the AMI treatment plan. Studies that analysed the same cohort were also excluded to avoid duplication of results.

A search of MEDLINE and EMBASE was performed on OVID using the search terms “Tei index” “myocardial performance index” “acute coronary syndrome” “acute myocardial infarction” “STEMI” in April 2020. The search results were independently reviewed for inclusion by two reviewers (SB and CSK). Full text of potentially relevant studies were downloaded and reviewed for final inclusion. Data extractions were performed by two independent reviewers (SB and CSK). Extracted information included study design, year, country the study was conducted in, number of participants, mean age of participants, percentage of male participants, participant inclusion criteria, echocardiographic findings, prognostic outcomes / clinical outcomes of Tei index. The Newcastle-Ottawa quality assessment scale was used to assess the quality of each included study.21 The Newcastle-Ottawa scale was incorporated into this review as it enables a standardised and comprehensive assessment of nonrandomised studies to be quality assessed against.21 Results from the extractions are presented in Tables. The results were narratively synthesized.

Results

Our search results yielded 144 potential inclusions and after detailed screening and review a total of 16 studies were included in the review (Figure 2).6,14-20, 22-29 These studies included 14 cohort studies and 2 matched control studies (Table 1). 15 out of the 16 studies that reported when the studies had been conducted showed that the studies were performed between 1995 to 2015. The studies took place around the world including Denmark, Norway, Egypt, Japan, Israel, Brazil, Poland, Turkey, Sweden and Romania. Overall, there were a total of 2886 participants with individual study participant numbers ranging from 44 to 417. From 14 studies that reported mean age of participants, the average overall age was 60 years. From 14 studies which reported participant sex, the overall mean percentage of male participants was 69.8%. Only 7 of the 16 included studies, included patients with first AMI. Detailed echocardiographic parameters that were reported in each of the included studies is shown in Table 2.
All studies used transthoracic echocardiography to assess Tei index, 3 of which used tissue Doppler image with the remaining studies using trans-mitral and left ventricular outflow time intervals obtained from either continuous or pulsed wave Doppler studies. Of the 16 studies, 10 included all coronary territory AMI patients, 2 studies included only anterior AMI patients, 1 included only anteroseptal AMI patients, the 3 studies did not comment on coronary territory. 12 studies indicated that the Tei index measurements were undertaken during the same hospitalisation of the AMI. However, the timing of the Tei index measurement in relation to the AMI event varied within 1 hour of the angioplasty procedure to within 7 days of AMI. Table 3 shows the quality assessment which was undertaken on all of the included studies in this review. The Newcastle-Ottawa Quality assessment tool indicated that 3 out of 16 studies were of fair quality while the remaining studies were of good quality. Of the 16 included studies, 14 studies indicated that a high Tei index value showed a significant association with heart failure episodes, re-infarction, death and left ventricular thrombus (see Table 4). These are discussed separately below.

**Tei index and mortality studies**

In the study by Karvounis et al, Tei index was greater among patients with Killip class II-III compared to Killip class I at both 1 day follow up and 1 month follow up. The mortality rate at 1 year was higher with Killip class II-III compared to class I.24 For survival, Moller et al found that survival at 1 year was 89% among patients with a Tei index <0.63 compared to 37% with a Tei index ≥0.63. Here, Tei index was associated with an increased risk of cardiac death (RR 5.6 95%CI 2.4-13.0).15 Moller et al also showed that at a median follow-up duration of 34 months, relative to a Tei index of <0.46, there was a 2 fold increase in risk of death with a Tei index value of between 0.46-0.68 and a 4-fold increase in risk of death with a Tei index value >0.68.15 Szymanski et al found that a Tei index >0.55 was associated with a 4-fold increase in risk of cardiac death and nonfatal recurrent myocardial infarction.14 Uzunhasan et al found that Tei index was greater among patients with death and heart failure.26

**Tei index heart failure studies**

Abuomara et al evaluated the value of a Tei index >0.73 compared to a LVEF ≤33% and found that the Tei index was more sensitive (78.3% vs 56.5%) with similar specificity (94.6% vs 94.6%) for in-hospital heart failure after AMI.6 Sasao et al concluded that a greater Tei index (reported as >0.70) was correlated with the development of heart failure episodes (OR 14.139 95%CI 1.269-157.553).18 Schwammenthal et al found that Tei index ≥0.52 was not predictive of adverse outcomes whilst an LVEF <40% was associated with adverse outcomes.19 Souza et al found that an LVEF ≤45% was associated with increased odds of in-hospital heart failure but only amongst patients ≥60 years of age with a Tei index ≥0.57.25
Tei index and composite adverse outcomes

Biering Sorensen et al reported that a greater Tei index value (0.59±0.16 Vs 0.52±0.13, \(P<0.001\)) was associated with major adverse outcomes including congestive heart failure, re-infarction and mortality.\(^{22}\) Similarly, over a 2 year follow up duration Hole et al found that Tei index was a better predictor of major adverse outcome compared to baseline LVESI and EDT but Tei index was not a better predictor of heart failure or death.\(^{23}\) Rahman et al found that a Tei index value >0.40 had better sensitivity (86% vs 65%), specificity (82% vs 50%) and accuracy (83% vs 58%) compared to LVEF <40% for predicting cardiac complications including cardiogenic shock, revascularisation, readmissions, congestive heart failure and advanced atrioventricular heart block.\(^{17}\) Westholm et al found that Tei index did not have a better AUC for predicting adverse outcomes compared to Simpson’s biplane LVEF.\(^{20}\) In the evaluation of left ventricular intra-cavity thrombus formation, Yilmaz et al reported that a Tei index value >0.60 had good sensitivity (81%) and specificity (73%) and was significantly predictive of thrombus formation when compared to ejection fraction. Yuasa et al found that the AUC analysis of a Tei index value ≥0.59 had similar AUC as ejection fraction <45% for 30-day complications.\(^{27}\) Zamfir et al found that RV Tei index was the only parameter which significantly correlated with reinfarction, need for revascularization and heart failure and death during the AMI hospitalisation (OR 9.17 95%CI 1.03-83.7).\(^{29}\)

Discussion

Our review on Tei index and its predictive value in morbidity and mortality events in AMI patients has several key findings. First, several studies indicate that a greater Tei index value can predict morbidity and mortality events during both the initial hospitalisation period and follow-up period ranging from 30 days to 57 months. Second, there is no consistency of what constitutes a greater, or abnormal, Tei index value. The most appropriate timing of Tei index evaluation is also not known. Thirdly, it is not certain whether the use of the Tei index has any advantage over the more utilised echocardiographic measurement of LVEF and more recent addition of global longitudinal strain imaging. More studies are needed in order to better understand Tei index before its routine incorporation into every day clinical practice.

The studies included in this review had several key differences making it challenging to assess the prognostic value of Tei index in AMI patients. Suggesting an appropriate “abnormal” cut off value for Tei index is challenging for a number of reasons. Firstly, in this review Tei index values were assessed at varying times throughout the initial hospitalisation period with differing “abnormal” cut of values being applied. Even in the five studies,\(^{6, 19, 24, 26, 27}\) where Tei index was assessed within 24 hours of AMI “abnormal” Tei index “abnormal” values ranged from >0.60,\(^{27}\) 0.686±0.12,\(^{24}\) >0.70,\(^{26}\) and >0.73.\(^{6}\) Identifying an appropriate
“abnormal” Tei index cut off range in AMI patients is also further compounded by the fact that the original research, whereby a normal Tei index value of <0.39±0.5 was derived, likely differs from the cohort of patients seem in this review. The original study by Tei et al,1 was based on a cohort of 170 adult participants, 70 of which had a normal LVEF, whereas the remaining 100 participants were known to have a dilated cardiomyopathy of varying severities (LVEF ranging from 30-50%), the breakdown of the underlying pathology however is not clear. Future studies are needed to clarify the optimal timing for when Tei index should be assessed along with systematically determining a Tei index “abnormal” cut off value which is best associated with adverse outcomes. The follow up duration also varied vastly from the inclusion of the initial hospitalisation period only right up to 58 months post AMI event. The use of different study end points was also apparent which included: mortality, re-infarction, left ventricular thrombus formation, tachyarrhythmia’s, bradyarrhythmia’s and heart failure episodes.

Current recommendations incorporate the use of LVEF and echocardiography assessment within 24-48 hours of an AMI which enables patients to be risk stratified and appropriately managed.9 Global longitudinal strain has also been shown to provide prognostic importance in AMI patients.30 However the use of LVEF via Simpson’s biplane and global longitudinal strain are reliant on adequate 2D endocardial border definition in non-foreshortened views. The Tei index is an easy measure of cardiac function which has the added advantage that it does not rely solely on adequate 2D image quality. This is important as Tei index could be used in patients where 2D / 3D LVEF or global longitudinal strain are impossible due to poor endocardial definition. Furthermore, LVEF is hinder by inter and intra observer variability, geometric assumptions, is pre and after-load dependent and is affected by the presence of variable and high heart rates.30 While there is limited evidence about the inter-observer variability of the Tei index measurements, the inter-observer variability is probably lower than that of either the left ventricular ejection fraction or global longitudinal strain measurements. Moreover, Tei index may be an attractive alternative quantification measurement as it has been shown to be independent of pre and after-load, heart rate and geometric assumptions.15 Thus, Tei index has the potential to be a more reproducible and reliable quantification measure with the added benefit of not being heavily reliance on endocardial definition and adequate 2D image quality. The appropriate timing of Tei index remains unknown, it is also unsure of whether a higher Tei index value would be required if evaluation is performed within the first 24-48 hours post AMI.

This review highlights the potential importance of an “abnormal Tei index value and its prognostic benefit to patients which is in keeping with the known prognostic value of Simpson’s biplane LVEF. There are some studies where the Tei index was found to be more sensitive, specific and accurate in comparison to LVEF in predicting morbidity and mortality events 6,17,27 however each of these studies differed in terms of study end points, follow up period as well as using differing Tei index cut off values. However, when a high Tei index
was considered together with a reduced LVEF, there were studies to suggested Tei index does not yield additional prognostic information over LVEF alone. Nevertheless, when the LVEF was greater than 45% its prognostic value to predict adverse outcomes reliably is limited. The measurement of a “abnormal” and high Tei index value in patients with mildly reduced or normal LVEF may highlight a previously undetected cohort of patients who are at a high risk of adverse events. Similarly, the finding of a reduced LVEF and low Tei index value may allow for further refinement in risk stratification of high-risk patients.

Studies have demonstrated myocardial recovery following an AMI event which can be easily detected with an improvement in Simpson’s biplane LVEF. There is limited information on whether Tei index showed a similar improvement over time. Hole et al and Karvounis et al were the only two studies which assessed Tei index at baseline and follow up the results of both indicated there to be no significant change. This was also irrespective of whether Tei index was high or not at base line. The clinical relevance of an improvement in Tei index over time remains unknown.

Karvounis et al was the only study to report on the individual components of Tei index. In this study, there was no change in the isovolumeric relaxation time at baseline and at one-month follow-up, this was irrespective of whether there were signs of heart failure or not in the included patient cohort. This study did not evaluate isovolumetric contraction.

This review highlights the small number of fair and good quality studies investigating Tei index in AMI patients. The strengths of the review are that it included only full studies with abstracts and case reports being excluded and all studies were prospective in design with well-defined patient outcome end points. Several studies included all coronary territory AMI events with only three studies being selective of anterior or anteroseptal AMI’s. This enables the results to be more applicable to a wider patient cohort. In addition, the studies are representative of the AMI cohort that is seen in clinical practice with a male predominance. Limitations of this review include the small sample sizes with the largest study involving 417 patients, there were large variations in follow up duration of patients. Patients were also managed differently which included being medically managed or receiving percutaneous coronary intervention which was performed either on admission or within 48 hours of AMI event.

Several questions remain unanswered related to the role of Tei index in patients with AMI. Future large prospective studies should aim to determine an acceptable “abnormal” cut off value for Tei index which is of a prognostic benefit to patients. The role of Tei index together with other measures such as 2D / 3D LVEF and global longitudinal strain analysis in post AMI patients merits further investigation over a short and long term follow up period.
The importance of a greater high Tei index value in patients with mildly impaired or a normal LVEF and a low Tei index value in patients with moderate or severely impaired LVEF should be investigated. In addition, the prognostic value of right ventricular myocardial performance in AMI patients should also be evaluated.

In conclusion, the studies in the literature suggest that the Tei index has value in identifying patients who have greater propensity for adverse events after AMI. However, more studies are needed to determine how Tei index should be used before its routine inclusion within clinical practice as there is uncertainly to its additional value over well-established parameters such as LVEF.

Declaration of interest, Funding and Acknowledgements:

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported. This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

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Figure 1: Schematic representation of Tei index

Figure 2: Flow diagram of studies inclusion
Figure 1. Schematic diagram of Tei index

Tei Index = \frac{A-B}{B} = \frac{ICT + IRT}{ET}

ICT - Isovolumetric contraction time
IRT - Isovolumetric relaxation time
Figure 2: Flow diagram of study inclusion

Search of MEDLINE and EMBASE yielded 144 studies.

Studies were excluded for the following reasons:

- 52 Conference abstracts.
- 1 Editorial.
- 68 studies not involving acute ST myocardial infarction participants.
- 7 Animal studies.

16 studies included.
| Study ID       | Study design; Country; Year                  | No. of Patients | Mean age | Male % | Inclusion criteria                                                                 | Exclusion criteria                                                                 |
|---------------|---------------------------------------------|----------------|----------|--------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Abuomara 2018 | Prospective cohort study; Egypt; 2014-2015  | 60             | 54       | 70     | Patients with first acute anterior STEMI treated with primary PCI.                   | Known dilated cardiomyopathy, previous PCI or CABG, non-sinus rhythm.               |
| Biering-Ørensen 2013 | Prospective cohort study; Denmark; 2006-2008 | 386            | 62       | 75     | Patients with STEMI treated with primary PCI.                                       | Poor quality echocardiography images.                                              |
| Hole 2003     | Prospective cohort study; Norway; 1995-1997. | 71             | 65       | 73     | Patients in sinus rhythm with AMI without heart failure.                             | Unstable angina requiring PCI, CABG, heart failure, AF, comorbid non-cardiac disease reducing life expectancy <2 years. |
| Karvounis 2004| Matched control study; Greece; unclear.      | 68             | 53       | 78     | Patients who survived AMI who received thrombolysis.                                | Previous Q wave myocardial infarction, AF, moderate to severe mitral regurgitation, severe aortic stenosis. |
| Møller 2001   | Prospective cohort study; Denmark; unclear. | 125            | 68       | Unclear | Patients with first AMI.                                                            | Aortic stenosis, implanted pacemaker and dementia.                                 |
| Møller 2003   | Prospective cohort study; Denmark; 1998-1999. | 799            | Median 69| 68     | Patients with definite AMI                                                          | Incomplete Doppler echocardiography.                                               |
| Rahman 2009   | Prospective cohort study; Pakistan; 2006-2007. | 202            | Unclear  | 78     | Patients with AMI.                                                                 | Significant mitral regurgitation or aortic stenosis, inadequate echo images, congenital heart disease. |
| Sasao 2004    | Matched control study; Japan; 2000-2001.    | 53             | 63       | 72     | Patients with first AMI treated with primary PCI.                                   | Slow flow after post PCI, presence of mechanical complications, previous myocardial infarction, AF, CABG, recent PCI, inadequate recording of echocardiography. |
| Schwammenthal 2003 | Cohort study; Israel; unclear.                | 417            | 62       | 78     | Patients with AMI.                                                                 | Patients who did not have echo evaluation.                                          |
| Souza 2011    | Prospective cohort study; Brazil; unclear.   | 95             | 58       | 67     | Patients with first STEMI                                                           | Previous AMI, early re-infarction, early re-infarction, in-hospital death, previous CABG or PCI, left bundle branch block, non-sinus rhythm, valvular heart disease, dilated cardiomyopathy, poor echocardiography images. |
| Szymanski 2002| Prospective cohort study; Poland; unclear.   | 90             | 58       | 71     | Patients who were hospital survivors of AMI.                                       | AF, sinus tachycardia, significant mitral/aortic stenosis/regurgitation, inadequate echocardiography studies. |
| Uzunhasan 2006 | Prospective cohort study;                    | 77             | 53       | 75     | Patients with transmural                                                             | AF, permanent pacemaker, dementia, aortic                                             |
| Study              | Design                  | Country          | Year Range      | Patients | Age Mean | Age SD | Diagnosis                                                                 |
|--------------------|-------------------------|------------------|-----------------|----------|----------|--------|-------------------------------------------------------------------------|
| Westholm 2013      | Prospective cohort study; Sweden; 2006-2008. | Turkey           | 2001-2002       | 227      | 67       | 76     | Patients admitted with an AMI.                                          |
| Yilman 2004        | Prospective cohort study; Turkey; unclear.       | Turkey           | 2006-2008       | 92       | 58       | 88     | Patients with first anterior AMI.                                        |
| Yuasa 2005         | Cohort study; Japan; unclear.                    | Japan            | 2004            | 80       | 64       | 78     | Patients with first anteroseptal AMI.                                   |
| Zamfir 2016        | Prospective cohort study; Romania; 2015-2016.    | Romania          | 2015-2016       | 44       | 63       | 70     | Patients with acute STEMI treated with primary PCI.                     |

Abbreviations – PCI: Percutaneous coronary intervention, AMI: Acute myocardial infarction, AF: Atrial fibrillation, STEMI: ST elevation myocardial infarction, CABG: Coronary artery bypass graft
Table 2: Supplementary echocardiogram parameters reported

| Study ID        | Echo parameters                                                                 |
|-----------------|----------------------------------------------------------------------------------|
| Abuomara 2018   | Overall Tei index mean 0.69±0.2. Overall EF mean 38.06±6.0%                     |
|                 | Comparing HF (n=23) with no HF (n=37):                                          |
|                 | Tei index: mean 0.88±0.18 vs 0.58±0.11, p=0.0001                               |
|                 | LVEF (%): mean 33.91±5.37% vs 40.64±4.86%, p=0.0001                           |
| Biering-Ørensen 2013 | Comparing no major adverse outcomes (n=290) to major adverse outcomes (n=96):   |
|                 | LVEF (%): 47±8 vs 41±9, p<0.001                                                |
|                 | Global longitudinal strain: -12.8 ±3.7 vs -10.4±3.5, p<0.001                   |
|                 | Tei index: 0.52±0.13 vs 0.59±0.16, p<0.001                                      |
|                 | LVIDd/BSA (cm/m²): mean 2.4 vs 2.6, p<0.001                                     |
|                 | LVESV/BSA (mL/m²): median 25 vs 29, p<0.001                                     |
|                 | LVMi (g/m²): mean 88 vs 102, p<0.001                                            |
|                 | LAVI (mL/m²): 25±7 vs 25±7, p=0.81                                              |
|                 | E velocity (m/s): 0.77±0.18 vs 0.77±0.24, p=0.83                               |
|                 | A velocity (m/s): 0.74±0.19 vs 0.75±0.23, p=0.68                               |
|                 | E/A ratio: 1.09±0.37 vs 1.09±0.37, p=0.95                                       |
|                 | DT (msec): 199±59 vs 201±75, p=0.80                                             |
|                 | e': 7.6±2.2 vs 6.7±1.9, p<0.001                                                |
|                 | E/e': 10.3 (8.1–12.4) vs 11.4 (9.1–14.4), p=0.002                              |
|                 | IVRT (msec): 101±21 vs 105±28, p=0.31                                           |
|                 | IVCT (msec): 30±14 vs 35±14, p=0.004                                            |
|                 | ET (msec): 258±30 vs 241±42, p<0.001                                            |
|                 | IVRT/ET (msec): 0.40±0.10 vs 0.44±13, p<0.001                                   |
|                 | IVCT/ET (msec): 0.12±0.06 vs 0.15±0.07, p<0.001                                |
|                 | Tei index: 0.52±0.13 vs 0.59±0.16, p<0.001                                      |
| Hole 2003       | Comparing baseline vs 2 years:                                                  |
|                 | LVEDVi (mL/m²): 95 (24) vs 104 (35), p=0.001                                    |
|                 | LVESVi (mL/m²): 52 (19) vs 59 (30), p=0.010                                     |
|                 | LVEF (%): 0.46 (0.07) vs 0.46 (0.09), not significant                           |
|                 | LVETI (msec): 413 (24) vs 430 (26), p<0.0005                                    |
|                 | E wave max velocity (cm/sec): 66 (15) vs 67 (15), not significant              |
|                 | E wave velocity time integral (cm): 10.9 (3.4) vs 13.6 (3.3), p<0.0005        |
|                 | A wave max velocity (cm/sec): 66 (21) vs 72 (20), p=0.001                      |
|                 | A wave velocity time integral (cm): 5.4 (2.0) vs 6.8 (2.1), p<0.0005           |
| E/A 1.09 (0.41) vs 1.05 (0.58), not significant |
| E wave DT (msec): 174 (52) vs 236 (72), p<0.0005 |
| DT of diastolic pulmonary vein flow (msec): 259 (71) vs 316 (88), p<0.0005 |
| Si/Si + Di: 0.58 (0.11) vs 0.58 (0.13), not significant |
| Diff Adur (msec): −0.41 (27) vs −21 (34), p<0.0005 |
| Tei index: 0.45 (0.14) vs 0.43 (0.16), not significant |

Karvounis 2004
Compared control (n=35) vs Killip class I (n=22) vs Killip Class II-III at day 1 (n=11):
- LVEF (%): 64.2±4.3 vs 59.3±6.7 vs 36.8±4.5, p<0.0001
- LVEDVi (mL/m²): 66.4±7.1 vs 68.2±6.5 vs 72.3±8.2, not significant
- LVESVi (mL/m²): 24.3±3.6 vs 28.4±3.9 vs 46.2±8.4, p<0.001
- WMSI: 1.00 vs 1.58±0.06 vs 1.88±0.35, p<0.05
- E wave (m/sec): 0.728±0.300 vs 0.732±0.150 vs 0.820±0.200, not significant
- A wave (m/sec): 0.520±0.220 vs 0.632±0.150 vs 0.578±0.240, not significant
- DT (msec): 0.164±0.020 vs 0.160±0.030 vs 0.127±0.027, not significant
- IVRT (msec): 0.090±0.030, 0.089±0.016 vs 0.090±0.027, not significant
- Tei index: 0.330±0.080 vs 0.344±0.084 vs 0.686±0.120, p<0.0001

Møller 2001
Compared survivors (n=90) vs non-survivors (n=35):
- LVEF (%): 0.57±0.14 vs 0.43±0.15, p<0.0001
- Wall motion score index: 1.41±0.27 vs 1.66±0.34, p<0.0001
- LVESVi (mL/m²): 29±17 vs 40±21, p<0.0001
- LVEDVi (mL/m²): 64±18 vs 68±23, not significant
- E/A ratio: 1.1±0.5 vs 2.0±1.6, p<0.004
- IVRT (msec): 88±28 vs 84±28, not significant
- IVCT (msec): 54±26 vs 82±51, p=0.005
- Ejection time (msec): 272±38 vs 217±42, p<0.0001
- E wave deceleration (msec): 212±60 vs 159±64, P<0.0001

Møller 2003
Compared survivors (n=602) vs non-survivors (n=197):
- WMSI: 1.6 vs 1.3, p<0.0001, RR 1.5 (1.4-1.7) (per 0.3 WMSI unit decrease)
- Tei index by quartiles:
  - Tei <0.46: (182/602 vs 19/197), RR 1.
  - Tei 0.46-0.55: (164/602 vs 36/197), RR 2.1 (1.2-3.5), p=0.01.
  - Tei 0.56-0.68: (148/602 vs 52/197), RR 3.0 (1.8-5.1), p<0.0001.
  - Tei >0.68: (108/602 vs 90/197), RR 6.4 (3.9-10.5), p<0.0001
- Impaired relaxation: 84/602 vs 27/197, RR 1.6 (1.1-2.5), p=0.02
- Restrictive filling: 82/602 vs 85/197, RR 4.1 (3.0-5.5), p<0.0001

Rahman 2009
Tei index >0.40 found in 90.6% of patients

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| Study           | Sample Description                                                                 | Findings                                                                 |
|-----------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| LVEF <50% found in 98% of patients | Sasao 2004 Compared controls (n=10) vs acute myocardial infarction patients (n=43): WMSI: not reported vs 1.45±0.18 E/A ratio: 0.82±0.19 vs 0.77±0.29, not significant DT (msec): 215±40 vs 184±43, p=0.043 Tei index: 0.375±0.036 vs 0.630±0.106, p=0.0001 |
| Schwammenthal 2003 Group A (no endpoint outcomes, n=314) vs group B (poor outcomes, n=103): LVEDD (cm): 5.0±0.5 vs 5.1±0.6, p=0.27 LVESD (cm): 3.3±0.6 vs 3.6±0.6, p=0.002 LVEDVi (mL/m2): 67±20 vs 70±20, p=0.23 LVESVi (mL/m2): 37±15 vs 42±16, p=0.002 LVEF (%): 46±9 vs 40±10, p<0.0001 Stroke distance (cm): 19±4 vs 17±4, p<0.0001 E/A 1.1±0.5 vs 1.3±1.1, p=0.002 DT (msec): 174±36 vs 157±35, p<0.0001 Tei index: 0.43±0.16 vs 0.50±0.22, p=0.0023 Isovolumetric time / heterovolumic time ratio: 0.18±0.08 vs 0.22±0.11, p<0.0001 |
| Souza 2011 Absence of early HF ( n=66) vs presence of early HF (n=29): LVEF (%): 0.51±0.07 vs 0.44±0.07, p<0.001 WMSI: 1.57±0.31 vs 1.91±0.35, p<0.001 LVESVi (mL/m2): 18.4±7.6 vs 20.8±8.7, p=0.18 LVEDVi (mL/m2): 37.3±12.2 vs 37.0±11.0, p=0.88 LAVi (mL/m2): 18.7±4.8 vs 20.6±5.7, p=0.10 E/A: 1.02±0.35 vs 0.99±0.50, p=0.76 DT (msec): 210±61.9 vs 212.7±66.8, p=0.85 Tei index: 0.57±0.14 vs 0.65±0.16, p=0.01 ET (msec): 262.3±22.8 vs 247.5±31.8, p=0.03 IVCT (msec): 46.5±24.2 vs 49.5±27.3, p=0.60 IVRT (msec): 102.0±26.6 vs 108.4±29.4, p=0.29 Diastolic pattern: normal 28/66 vs 5/29, p=0.06, abnormal relaxation 27/66 vs 14/29, pseudo-normal 7/66 vs 6/29, restrictive 4/66 vs 4/29 |
| Szymanski 2002 Univariate RR for predicting cardiac events (cardiac deaths or nonfatal recurrent MI) according to echocardiographic parameters: WMSI >1.3: RR 2.10 (0.76-5.75), p=0.15 LVEF (%): ≤40%: RR 3.00 (1.28-7.03), p=0.01 LVESV (mL): >65 mL: RR 3.79 (1.62-8.90), p=0.002 ET (msec): ≤0.240 sec: RR 3.40 (1.47-7.89), p=0.004 DT (msec): ≤0.145 sec: RR 2.84 (1.21-6.67), p=0.02 |
| Study                  | Comparison                                           | LVDD (cm)         | LVSD (cm)         | LVEDV (cm²)       | LVESV (cm²)       | LVEF (%)         | E wave (cm/sec) | A wave (cm/sec) | DT (msec)  | IVRT (msec) | IVCT (msec) | ET (msec)   | Tei index |
|------------------------|------------------------------------------------------|-------------------|-------------------|-------------------|-------------------|----------------|----------------|----------------|------------|-------------|-------------|------------|----------|
| Uzunhasan 2006         | Compared AMI patients (n=77) vs controls (n=88):     | 5.1±0.5 vs 4.7±0.4 | 3.5±0.7 vs 2.8±0.5 | 123.0±23.7 vs 101.3±22.4 | 69.1±23.0 vs 35.9±11.0 | 44.1±9.0 vs 69.2±6.9 | 0.6±0.2 vs 0.9±0.2 | 0.6±0.1 vs 0.7±0.4 | 162.5±0.4 vs 196.1±32.2 | 78.4±9.9 vs 83.4±9.9 | 76.1±16.6 vs 43.9±11.0 | 252.6±35.5 vs 326.1±21.0 | 0.63±0.1 vs 0.39±0.03 |
| Westholm 2013          | All vs (no death, MI or HF) vs (death, MI or HF), median (25th-75th percentile): | 49 (41-56) vs 45 (35-52) vs 52 (45-58), p<0.001 | 1.06 (1.00-1.33) vs 1.14 (1.00-1.56) vs 1.00 (1.00-1.16), p<0.001 | 41.0 (33.0-50.0) vs 50.0 (44.0-58.0), p<0.001 | 1.33 (1.0-1.63) vs 1.0 (1.9-1.2), p<0.001 | 13.7 (8.7-22.1) vs 7.6 (3.1-13.7), p<0.001 | 45.0 (35.0-52.0) vs 52.0 (45.0-58.2), p<0.001 |
Global strain: -11.2 (-14.5 -7.8) vs -14.6 (-16.7-12.3), p<0.001
Post systolic index: 11.3 (5.1-18.7) vs 7.6 (3.3-13.4), p=0.007

**MI vs no MI, median (25th -75th percentile):**

Septal –lateral delay: 28.0 (0.0-73.8) vs 20.0 (0-111.2), p = 0.629
Post systolic index SD: 16.2 (9.7-30.1) vs 12.5 (6.1-20.3), p=<0.009
Post systolic index delta: 55.5 (34.3-102.3) vs 41 (21-67), p=<0.019
Time to peak 2D-strain SD: 0.032 (0.016-0.068) vs 0.017 (0.009-0.047), p=0.019
Time to peak 2D- strain delta: 0.10 (0.050-0.23) vs 0.057 (0.026-0.17), p=0.030
Tei index SD: 0.16 (0.09-0.24) vs 0.14 (0.09-0.20), p=0.117
Tei index delta: 0.41 (0.24-0.58) vs 0.33 (0.23-0.50), p=0.074
LVEF (%): 44.0 (35-52) vs 51 (43-58), p=0.002

**WMSI: 1.22 (1.0-1.54) vs 1.00 (1.00-1.16), p=0.026**

**Post systolic index delta: 55.5 (34.3-102.3) vs 41 (21-67), p=0.007**

**Tei index SD: 0.16 (0.09-0.24) vs 0.14 (0.09-0.20), p=0.117**

**Tei index delta: 0.41 (0.24-0.58) vs 0.33 (0.23-0.50), p=0.074**

**LVEF (%): 44.0 (35-52) vs 51 (43-58), p=0.002**

**Composite end point of death and readmission due to HF vs endpoint not met, median (25th -75th percentile):**

Lateral delay: 28 (0.00-94.0) vs 18.0 (0.00-107.2), p=0.111
Septal – lateral delay: 25 (0-84) vs 18.5 (0-.69.3), p=0.387
Post systolic index SD: 19.9 (11.5-28.7) vs 12.4 (6.7-18.2), p=0.001
Post systolic index delta: 66.0 (32.0-103.0) vs 41.0 (22.0-53.5), p=0.001
Time to peak 2D-strain SD: 0.041 (0.17-0.66) vs 0.14 (0.007-0.032), p=0.001
Time to peak 2D-strain delta: 0.14 (0.049 -0.24) vs 0.044 (0.023-0.116), p=0.001
Tei index SD: 0.17 (0.12-0.24) vs 0.13 (0.088-0.19), p=0.001
Tei index delta: 0.42 (0.32-0.60) vs 0.33 (0.22-0.48), p=0.0011
LVEF (%): 41.0 (33.7-51.0) vs 52.0 (45.5-63.2), p=0.001
Global strain: -10.9 (-14.6 -7.7) vs -14.4 (-16.6 -11.4), p=0.002
WMSI: 1.22 (1.0-1.54) vs 1.00 (1.00-1.16), p=0.026
Post systolic index: 10.3 (7.00-24.7) vs 8.7 (3.9-15.3), p=0.058

**Tei index SD: 0.16 (0.09-0.24) vs 0.14 (0.09-0.20), p=0.117**

**Tei index delta: 0.41 (0.24-0.58) vs 0.33 (0.23-0.50), p=0.074**

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Tei index SD: 0.17 (0.12-0.24) vs 0.13 (0.088-0.19), p=0.001
Tei index delta: 0.42 (0.32-0.60) vs 0.33 (0.22-0.48), p=0.0011
LVEF (%): 41.0 (33.7-51.0) vs 52.0 (45.5-63.2), p=0.001
Global strain: -10.9 (-14.6 -7.7) vs -14.4 (-16.6 -11.4), p=0.002
WMSI: 1.22 (1.0-1.54) vs 1.00 (1.00-1.16), p=0.026
Post systolic index: 10.3 (7.00-24.7) vs 8.7 (3.9-15.3), p=0.058

**LVESV (mL): 82±20 vs 61±16, p<0.001**

**LVEDV (mL): 130±38 vs 118±35, p=0.124**

**LVEF (%): 37±6 vs 47±9, p<0.001**

**E (cm/s): 72±13 vs 58±15, p<0.001**

**A (cm/s): 49±17 vs 71±22, p<0.001**

**E/A: 1.60±0.62 vs 1.00±0.50, p<0.001**

**DT (msed): 138±24 vs 220±51, p=0.001**

**IVRT (msed): 77±22 vs 96±16, p<0.001**

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**Yilman 2004**

LV thrombus vs no LV thrombus:

WMSI: 2.27±0.33 vs 1.77±0.27, p<0.001
LVESV (mL): 82±20 vs 61±16, p<0.001
LVEDV (mL): 130±38 vs 118±35, p=0.124
LVEF (%): 37±6 vs 47±9, p<0.001
E (cm/s): 72±13 vs 58±15, p<0.001
A (cm/s): 49±17 vs 71±22, p<0.001
E/A: 1.60±0.62 vs 1.00±0.50, p<0.001
DT (msed): 138±24 vs 220±51, p=0.001
IVRT (msed): 77±22 vs 96±16, p<0.001
| Study          | Results                                                                                           |
|---------------|--------------------------------------------------------------------------------------------------|
| **Yuasa 2005** | No complications (LV aneurysm, congestive HF, shock, paroxysmal AF, cardiac death, VT/VF, pericardial effusion, cardiac rupture, advanced AV block) (n=49) vs with complications (n=31):  
  LVEF (%): 52±10 vs 44±8, P<0.001  
  WMSI: 1.64±0.28 vs 1.93±0.3, P<0.0001  
  E/A: 0.98±0.46 vs 0.98±0.59, not significant  
  Mitral E DT (msec): 164±46 vs 153±93, no significant  
  Tei index: 0.50±0.11 vs 0.69±0.16, P=0.0001  |
| **Zamfir 2016** | MACE (n=12) vs MACE free (n=32) events.  
  LVEF (%): 40.50±8.79 vs 46.14±8.36 – not stated  
  TAPSE (cm): 19.33±4.71 vs 19.71±3.78 p*=-0.439, p**=<0.001  
  S wave velocity (cm/sec): 0.130±0.28 vs 0.136±0.27, p*=-0.539, p**=0.004  
  RV longitudinal strain: -20.83±12.26 vs -21.27±13.21, p*0.965, p**=0.024  
  RV fractional area change (%): 40.66±9.35 vs 42.74±8.67, p* 0.810, p** <0.001  
  RV Ejection fraction: 42.56±8.43 vs 46.00±9.63, p*0.807, p**0.001  
  RV Tei index: 0.582±0.22 vs 0.588±0.10, p*0.037, p** <0.001  |

Abbreviations - RV: Right ventricle / right ventricular AV: atrioventricular, LVEF: left ventricular ejection fraction, MACE: major adverse cardiac events, LV: left ventricle / left ventricular, S: systolic component of pulmonary venous flow, IVRT: isovolumetric relaxation time, IVCT: isovolumetric contraction time, DT: deceleration time, LVEDV: left ventricular end diastolic volume, LVESV: left ventricular end systolic volume, Si/Si + Di: systolic fraction of total forward integral, LVEDVi: left ventricular end diastolic volume index, LVESVi: left ventricular end systolic volume index, WMSI: wall motion score index, MI: myocardial infarction, HF: heart failure, ET: ejection time, LVSD: left ventricular systolic dimension, LVEDV: left ventricular end diastolic volume, LAVI: left atrial volume index, LVMI: left ventricular mass index, BSA: Body surface area, VT: ventricular tachycardia, VF: ventricular fibrillation, AF: atrial fibrillation, TAPSE: Tricuspid annular plane systolic excursion, E:early left ventricular filling wave, A: active left ventricular filling wave, SD: standard deviation, msec: milliseconds.
Table 3: Study quality assessment using Newcastle Ottawa Scale

| Study ID         | Timing of Tei index measurements                                                                 | Selection domain | Comparability domain | Outcome domain*** | Overall   |
|------------------|--------------------------------------------------------------------------------------------------|------------------|----------------------|-------------------|-----------|
| Abuomara 2018    | Within 24 hours of presentation                                                                 | ****            | *                    | **                | Good quality |
| Biering-Sørensen 2013 | Within 5 days of admission                                                                   | ***             | **                   | ***               | Good quality |
| Hole 2003        | Between 2 and 7 days after AMI                                                                  | ***             | -                    | **                | Fair quality |
| Karvounis 2004   | Within 24 hours of admission and repeated 1 month after AMI                                    | ***             | *                    | **                | Good quality |
| Möller 2001      | Within 24 hours of admission, then on day 5, 1 & 3months post AMI                               | ***             | -                    | *                 | Fair quality |
| Möller 2003      | Within 6 days of AMI                                                                            | ****            | *                    | ***               | Good quality |
| Rahman 2009      | Unclear                                                                                         | ***             | -                    | **                | Good quality |
| Sasao 2004       | Within 1 hour of angioplasty                                                                    | ***             | *                    | ***               | Good quality |
| Schwammenthal 2003 | Within 24 hours of hospital admission                                                           | ****            | *                    | ***               | Good quality |
| Souza 2011       | Within 24 hours of arrival at coronary care unit, within 48 hours of chest pain                | ***             | *                    | **                | Good quality |
| Szymanski 2002   | 14±2 days post AMI                                                                              | ***             | **                   | **                | Good quality |
| Uzunhasan 2006   | Within 24 hours of admission                                                                    | ***             | -                    | **                | Good quality |
| Westholm 2013    | Median time 3(2-4) days from admission                                                          | ***             | -                    | ***               | Good quality |
| Yilmaz 2004      | Within 24 hours of admission                                                                    | ***             | *                    | ***               | Good quality |
| Yuasa 2005       | At time of admission                                                                            | ***             | *                    | ***               | Fair quality |
| Zamfir 2016      | Within hospitalization stay of AMI                                                               | ***             | *                    | **                | Good quality |

Abbreviations - AMI: acute myocardial infarction, LV: left ventricle.

*Selection domain based on: 1) Representativeness of exposed cohort, 2) Selection of the non-exposed cohort, 3) Ascertainment of exposure, 4) Demonstration that outcome of interest was not present at the start of the study.

**Comparability domain based on: Comparability of cohorts on the basis of the design of analysis. Control for age=* , control for other factors=*. 

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***Outcome domain based on: 1) Assessment of outcome, 2) Was follow-up long enough for outcomes to occur, 3) Adequacy of follow up of cohorts.
Table 4: Tei index cut off values, outcomes and prognostic use of Tei index.

| Study ID       | Tei index abnormal cut off values | Tei index and outcomes                                                                 | Tei index prognostically useful?                                                                 |
|----------------|----------------------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Abuomara 2018  | >0.73                            | Tei Index with and without heart failure: 0.88±0.18 vs 0.58±0.11, p=0.0001. Heart failure with Tei Index >0.73: sensitivity 78.3%, specificity 94.6%. | Yes, able to predict development of heart failure                                                |
| Biering-Ørensen 2013 | 0.59±0.16                  | Tei Index with and without major adverse outcome: 0.59±0.16 vs 0.52±0.13, p<0.001.       | Yes, able to predict development of heart failure, future hospitalisation, re-infarction and mortality |
| Hole 2003      | N/A                              | Tei Index was a significant predictor of major adverse outcome, but not for the development of heart failure or death. | No, not able to predict heart failure episodes.                                                  |
| Karvounis 2004 | N/A                              | Control vs Killip class I vs Killip class II-III: Tei Index at day 1: 0.330±0.080 vs 0.344±0.084 vs 0.686±0.120, p<0.0001. Tei Index At 1 month: 0.330±0.080 vs 0.329±0.080 vs 0.649±0.110, p<0.0001. | Yes, associated with mortality.                                                                 |
| Møller 2001    | >0.63                            | One-year survival in patients with Tei Index <0.63 was 89% compared to 37% in patients with index ≥0.63, p<0.0001. Cardiac death with Tei Index >0.63: RR 5.6 (2.4-13.0), p<0.0001. | Yes, able to predict LV dilatation and mortality.                                                |
| Møller 2003    | N/A                              | Multivariable predictors of all-cause deaths according to Tei index: Tei index < 0.46: ref. Tei index 0.46-0.55: aRR 2.1 (1.2-3.6), p=0.001. Tei index 0.56-0.68: aRR 2.3 (1.5-3.9), p=0.001. Tei index > 0.68: aRR 4.0 (2.1-11.6), p<0.0001. | Yes, independent predictor of morality.                                                        |
| Rahman 2009    | >0.40                            | Prediction of cardiac complications: Tei index of >0.40 sensitivity 86%, specificity 82%, accuracy 83%. Tei Index and hazards ratios for complications: Cardiogenic shock: HR 2.5 (1.7-3.6), p=0.008. Cardiac death: HR 2.0 (1.4-2.9), p=0.30. Revascularization: HR 2.0 (1.6-2.7), p=0.023. Readmission: HR 1.3 (1.1-1.4), p=0.016. Congestive heart failure: HR 2.0 (1.6-2.7), p=0.041. Secondary arrhythmias: HR 1.5 (1.1-1.9), p=0.32. Advanced atrioventricular block: HR 1.4 (1.2-1.7), p=0.03. | Yes, independent predictor of cardiac complications (excluding secondary arrhythmia's). |
| Study            | Tei index Value | Description                                                                                     | Associated Outcomes                                                                 |
|------------------|-----------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Sasao 2004       | >0.70           | Tei index significantly higher in acute myocardial infarction patient’s vs controls: 0.630 vs 0.375, p<0.0001. Tei index >0.70 was significantly correlated with cardiac events (cardiac death or congestive heart failure): OR 14.139 (1.269-157.553), p=0.0313. | Yes, significantly associated with development of heart failure and mortality but only when LVEF <45% in patients >60 years. |
| Schwammenthal 2003 | >0.52          | Multivariable predictor of death, congestive heart failure and reinfarction: 
Tei Index ≥0.52: OR 1.09 (0.59-2.14).
LVEF <40%: OR 3.82 (2.15-6.87). | No, not able to predict development of heart failure, re-infarction or mortality. |
| Souza 2011       |                 | Independent predictor of in-hospital congestive heart failure events: 
Left ventricular ejection fraction ≤45%: OR 17.0 (4.1-70.8), p<0.0001. 
Age ≥60 and Tei index <0.57: OR 0.5 (0.1-4.1). 
Age ≥60 and Tei index ≥0.57: OR 13.7 (2.7-68.6), p=0.02 | Yes, independent predictor for development of in-hospital heart failure. |
| Szymanski 2002   | >0.55           | Cardiac deaths and nonfatal recurrent myocardial infarction with Tei index ≥0.55 aRR 4.45 (1.28-15.45), p=0.019. | Yes, independent predictor for mortality or re-infarction. |
| Uzunhasan 2006   | Heart failure: >0.76±0.27 
Mortality: 0.60±0.32 | AMI patients (n=77), controls (n=88) 
High (>0.60) vs low (<0.60) Tei index: 
Death: 12 (30.8%) vs 1 (2.6%). 
Heart failure: 19 (48.7%) vs 3 (7.9%). 
Mean Tei index of surviving vs dead patients: 0.61±0.1 vs 0.7±0.1, p=0.001. | Yes, indicator for development of heart failure, LV dysfunction and mortality. |
| Westholm 2013    | N/A             | ROC analysis with AUC for Tei Index SD vs Tei Index Delta vs Simpson LVEF in respect to death: 0.65 (0.56-0.74) vs 0.64 (0.55-0.73) vs 0.73 (0.65-0.81). | No, no significant prognostic information derived. |
| Yilmaz 2004      | >0.60           | Left ventricular thrombus formation prediction had a sensitivity of 81%, specificity of 73%, positive predictive value of 62%, negative predictive value of 88%. | Yes, able to predict development of LV thrombus. |
| Yuasa 2005       | >0.59           | Multivariate predictors of complications (left ventricular aneurysm, heart failure, shock, paroxysmal atrial fibrillation, cardiac death, ventricular tachycardia / ventricular fibrillation, pericardial effusion, cardiac rupture, advanced atrioventricular block). | Yes, able to predict complications of AMI. |
| Zamfir 2016      | N/A             | RV Tei index was the only parameter to correlated with major adverse cardiac events. | Yes, able to predict development of heart failure, re-infarction, need for re-vascularisation and mortality. |

Abbreviations - ROC: Receiver operating characteristics, AUC: Area under the curve.