

The prediction of death up to 100 days after admission to hospital for acute medical illness - the comparison of two ECG interpretation methods with ECG-dispersion mapping

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Abstract

Background: the prognostic performances of different ECG interpretation methods have not been compared.

Methods: the 100 day mortality of 513 patients predicted by Marquette proprietary ECG software, Tan et al's scoring system and the myocardial micro-alternation index (MMI) were compared.

Results: 33 patients (6.4%) died within 100 days of hospital admission. The c statistics for Marquette and Tan ECG interpretation and MMI were not statistically different (i.e. 0.64, 0.68 and 0.73, respectively). Only MMI was independent from age as a predictor of mortality. The c statistic for MMI plus age of 0.81 was significantly higher than that of Marquette ECG interpretation (p 0.015).

Conclusion: predictions of 100 day mortality by of all three ECG interpretation methods are equivalent.

Keywords:

prognostication, ECG, ECG dispersion mapping

Key points

- ECG dispersion mapping (ECG-DM) is a novel technique that analyzes low-amplitude ECG oscillations and reports them as the myocardial micro-alternation index (MMI).
- This study is the first to directly compare ECG-DM with the prognostic ability with conventional ECG interpretation methods
- Predictions of 100 day mortality by Marquette proprietary ECG interpretation software and the Tan ECG score are equivalent to those of ECG-DM. Combining MMI with patient age yields a score with excellent discrimination and goodness-of-fit.

Introduction

One of the main reasons patients get admitted to hospital is the fear that they may die. Prognostication is one of the lost arts of medicine, largely because it is not studied and what is known is poorly taught.¹ It is well established that a patient's prognosis depends on the severity of their illness (i.e. vital signs), the number of co-morbid conditions, and their functional status.² Surprisingly, however, in a cohort of nearly 10,000 patients admitted to our hospital we found that an abnormal ECG was the most powerful predictor of in-hospital mortality after a history of chronic illness, poor functional capacity and nursing home residence.³

Although numerous studies have demonstrated the prognostic value of electro-cardiograms (ECGs) for cardiac conditions,⁴⁻⁷ these reports have confined themselves to specific patient populations, and not to the type of unselected patients attending acute medical units. In our patient population we found only four out of 4177 acutely ill patients with an

ECG interpreted as normal by Marquette proprietary software died within 24 h, and the odds ratio for 30-day mortality for those with an abnormal ECG was 5.2 (95% CI 3.7–7.4, p <0.0001).^{3,8} In a separate study on much younger patients performed in Malawi,⁹ in which ECGs were interpreted independently by two researchers, the odds ratio of an abnormal ECG for in-hospital death was 2.08 (95% CI 1.12 – 3.88, p 0.02).

The performance of an ECG is time consuming and its interpretation, if proprietary software is not available, requires training and is prone to inter-observer error. Tan et al¹⁰ reported a simple score that awarded one point to each of 12 ECG abnormalities: left and right bundle branch block, diagnostic Q waves, intra-ventricular conduction defect, atrial fibrillation, left atrial abnormality, left and right axis deviation, left and right ventricular hypertrophy, ST depression, and an abnormal QTc interval. This simple score showed a progressive increase in the risk of death that was independent of age, standard risk factors, and clinical status.

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Table 1. Continuous variables

	Total	Survived 100 days	Died within 100 days	P
Patient number:	513	480	33	
Age (years)				
Mean	66.7 SD 18.6	65.6 SD 18.6	82.9 SD 7.2	<0.00001
Median	70	69	84	
Range	(14.0 – 99.0)	(14.0 – 99.0)	(69.0 – 99.0)	
Quartile	56.0 – 81.0	55.0 – 81.0	78.0 – 87.0	
Length of stay (days)				
Mean	4.5 SD 7.3	4.1 SD 7.1	10.8 SD 7.4	<0.00001
Median	2	2	9	
Range	(0.0 – 76.0)	(0.0 – 76.0)	(0.0 – 28.0)	
Quartile	0.0 – 6.0	0.0 -5.0	6.0 – 14.0	
Heart rate (bpm)				
Mean	78.3 SD 15.5	78.4 SD 15.6	77.5 SD 13.8	0.74
Median	76	76	78	
Range	(44 – 157)	(44 – 157)	(49 – 115)	
Quartile	67 - 88	67 - 88	66 – 85	
QRS (mV)				
Mean	89.7 SD 19.5	89.1 SD 17.8	98.5 SD 34.7	0.01
Median	86	84	88	
Range	46 – 226	46 – 216	62 – 226	
Quartile	78 - 96	78 – 96	78 – 104	
Axis (°)				
Mean	14.4 SD 38.0	15.2 SD 37.2	2.9 SD 46.2	0.07
Median	10	11	-3	
Range	(-85.0 – 110.0)	(-83 – 110.0)	(-85.0 – 80.0)	
Quartile	-13.0 – 42.0	-12.0 – 42.0	-25.0 – 39.0	
QTc (ms)				
Mean	436 SD 30	434 SD 29	457 SD 41	<0.00001
Median	432	432	453	
Range	(278 – 600)	(278 – 600)	(386 – 552)	
Quartile	416 - 452	416 - 450	427 - 488	
Tan score				
Mean	1.01 SD 1.27	0.95 SD 1.22	1.88 SD 1.60	0.00005
Median	1	1	1	
Range	0 – 6	0 – 6	0 – 6	
Quartile	0 - 2	0 – 1	1 – 3	
MMI (%)				
Mean	20.3 SD 11.4%	19.8 SD 10.9%	28.6 SD 14.1%	0.00001
Median	15	15	23	
Range	3 – 92 %	3 – 92%	12 – 53%	
Quartile	14 – 22%	14 – 21%	17 – 40%	

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Table 2. Prevalence of male gender, tachycardia, bradycardia and ECG abnormalities with their associated odds ratio for 100 day mortality.

	Percent of patients	Dead	Total	100 day Mortality (%)	Odds ratio (95%CI)		Chi square	P
LVH *	16.8%	8	86	9.3%	1.64	(0.65 – 4.03)	0.88	0.35
RVH *	0.2%	0	1	0.0%	0.00	(0.00 – 262.4)	3.14	0.08
RBBB *	4.9%	4	25	16.6%	3.00	(0.80 – 10.20)	2.48	0.12
LBBB *	2.5%	2	13	15.4%	2.74	(0.00 – 14.18)	0.57	0.45
IVCD >110 ms	9.6%	6	49	12.2%	2.25	(0.78 – 6.19)	2.04	0.15
Q waves *	6.4%	5	33	15.2%	2.87	(0.89 – 8.69)	3.01	0.08
ST depression >10 mV	4.7%	6	24	25.0%	5.68	(1.83 – 17.00)	11.29	0.001
Atrial fibrillation	10.2%	7	53	13.2%	2.53	(0.93 – 6.61)	3.30	0.07
Left atrial abnormality	4.5%	0	23	0.0%	0.00	(0.00 – 3.17)	0.73	0.39
LAD (-30° to -89°)	12.5%	8	64	12.5%	2.41	(0.94 – 6.00)	3.35	0.07
RAD (+90° to -289°)	1.8%	0	9	0.0%	0.00	(0.00 – 8.99)	0.01	0.91
Long QT (>450 ms)	27.1%	16	139	11.5%	2.72	(1.25 – 5.89)	6.96	0.01
Male gender	46.8%	19	240	7.9%	1.59	(0.74 – 3.44)	1.22	0.27
HR <51 bpm	1.4%	1	7	14.3%	2.47	(0.00 – 22.11)	0.01	0.94
HR >90 bpm	19.3%	7	99	7.1%	1.14	(0.43 – 2.88)	0.00	0.95

* full definitions of all ECG abnormalities provided in Reference [8]; ms = milliseconds; mV = millivolts; bpm = beats per minute.

ECG dispersion mapping (ECG-DM) is novel technology that only takes a few seconds to perform and requires little skill to interpret. It assesses myocardial pathology by analyzing not only the tiny fluctuations of the T-wave (T wave alternans) but also micro-fluctuations of the P wave and QRS complex. In health all ECG PQRST complexes are identical and could be perfectly superimposed on top of each other. In illness, however, there are slight differences in the PQRST complex from beat to beat, so that if they were superimposed on each other there would be small deviations visible. All these micro-deviations can be combined into one overall myocardial micro-alternation index (MMI) which is expressed as a percentage — if pathological micro-deviations are present throughout the entire myocardium the MMI is 100%, whereas an MMI of 0% indicates a total absence of abnormal micro-deviations.^{11,12} We have already reported ECG-DM can predict in-hospital mortality¹³ and combining MMI with patient age predicts of 1-year mortality.¹⁴

In this paper we define ECG abnormality and normality using Tan et al's non-proprietary scoring system, and compare its prognostic performance with that of Marquette proprietary software and ECG-DM

Methods

This study was performed at Nenagh Hospital from 11 January 2012 and 26 February 2014. Nenagh Hospital is a small general hospital in rural

Ireland serving a population of 60,000. Since its reconfiguration in 2010 it has a 49 bed medical unit to which approximately 2000 patients a year are admitted. Most patients are admitted after assessment in the hospital's medical assessment unit (MAU), which is open from 9 am to 5 pm from Monday to Friday. Outside of these hours patients are assessed in the hospital's emergency department. Since the hospital no longer has an intensive care unit, more seriously ill patients are usually taken by the ambulance to Limerick University Hospital, which is 30 miles away.

During the study period 2,105 admissions were assessed in the hospital's MAU: 638 (30%) of these admissions occurred while the author MC was working in the MAU and were, therefore, included in the study. These 638 admissions were of 513 individual patients, who were followed up for a minimum of 100 days after admission. All patients had a 12 lead ECG (Marquette MAC-PC) and ECG-DM (HeartVue system, Medical Computer Systems Ltd, Moscow) performed in the MAU at the time of admission. The ECG-DM device is a black box with four ECG limb leads at one end and a USB lead at the other that connects to any computer on which ECG-DM interpretation software is installed. An ECG-DM is performed by pressing a start button on the computer screen, and 30 seconds later the MMI is displayed. All MMI results are automatically data and time stamped and stored in the software's database.

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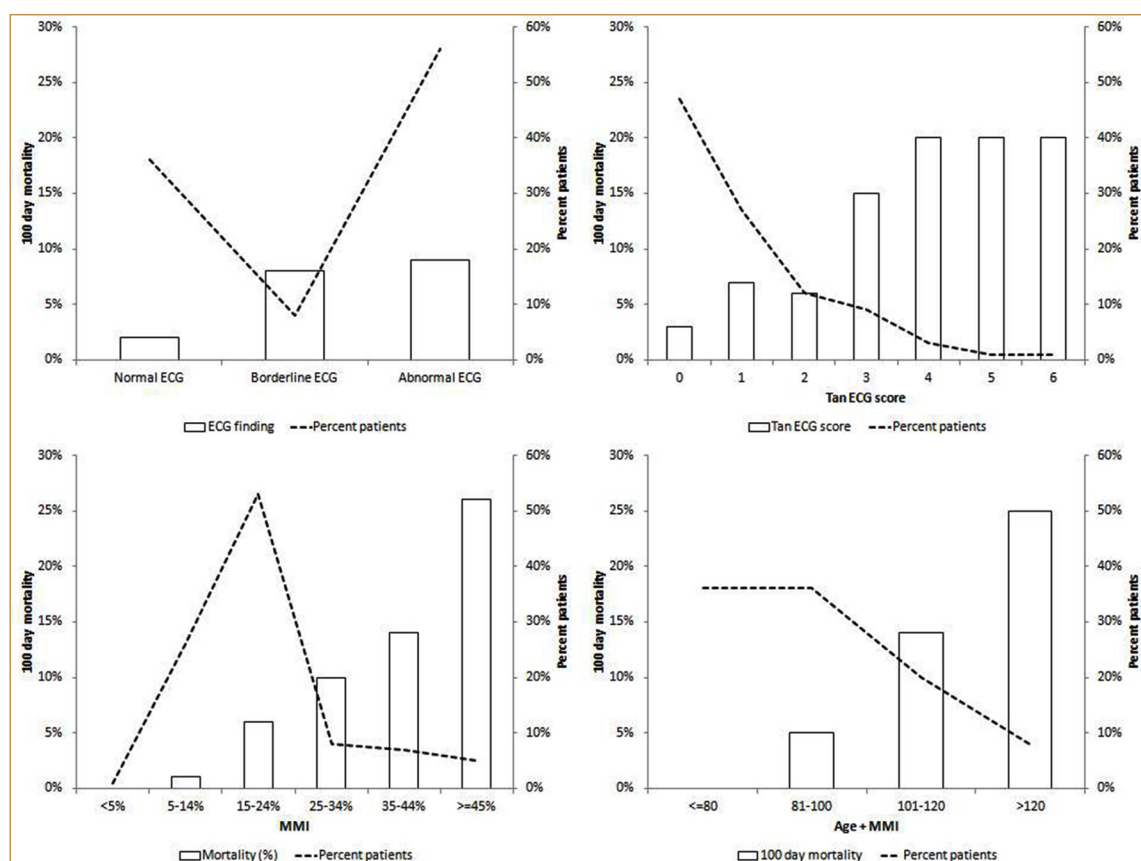


Figure 1. 100 day mortality according to different Marquette ECG interpretations, Tan ECG scores, and MMI and MMI plus age score values

For patients with more than one admission the ECG and ECG-DM used in the study was the one performed at the time of their first admission. The Tan ECG score was determined according to the published criteria⁸ by the author JK without knowledge of the patient's identity, clinical condition or outcome. Sinus tachycardia and bradycardia, as defined by heart rates faster or slower than those awarded a score of zero by the National Early Warning Score,¹⁵ were not considered to be ECG abnormalities.

Follow-up was performed by contacting the patient directly and/or their family doctor and/or reviewing the hospital's patient administration system for those patients still attending out-patient services. For those patients who had died, the exact date of death was obtained from the North Tipperary Registrar of Births Marriages and Deaths and/or the website rip.ie. No patient was lost to follow-up.

All statistical calculations were performed using Epi-Info version 7.0 (Center for Disease Control and Prevention, USA) or OASIS Online Application for the Survival Analysis software available at <http://sbi.postech.ac.kr/oasis/surv/>.¹⁶ The p value for statistical significance was <0.05, odds ratios were tested using Student's t-test and Chi square

analysis that applied Yates continuity correction and risk differences tested by Fisher's exact test. Kaplan-Meier survival curves were compared by the log-rank test. The c statistic of discrimination was calculated and compared according to the method of Hanley and McNeil.¹⁷ Ethical approval of the study was obtained from the Mid- Western Regional Hospital Complex Scientific Research Ethics Committee, which granted exemption for obtaining patient consent.

Results

Of the 513 patients studied, 33 (6.4%) died within 100 days of hospital admission. The patients who died had a longer length of hospital stay and were older than survivors, and none of them were under 69 years of age (Table 1). The commonest ECG abnormalities were a prolonged QT interval, left ventricular hypertrophy, left axis deviation and atrial fibrillation (Table 2). ECG findings that were significantly increased in patients who died were QRS and QT duration, the presence of ST changes, the Tan ECG score and the MMI (Tables 1 and 2).

There was no statistical differences between the 100 day mortality rates associated with Tan score of

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Table 3. Total patients and patients who died according Marquette ECG interpretation and Tan ECG score [Ref 8] by MMI value. Patients who died are in parentheses.

Marquette ECG	Tan score	MMI <15%	MMI 15-24%	MMI ≥25%	Total
Abnormal	0	25 (1)	45 (2)	8 (1)	78 (4)
	1-2	31 (0)	112 (9)	34 (4)	177 (13)
	≥3	3 (0)	14 (1)	54 (11)	71 (12)
	Total	60 (2)	172 (12)	97 (16)	326 (29)
Normal	0	72 (0)	84 (3)	5 (0)	161 (3)
	1-2	9 (0)	15 (1)	2 (0)	26 (1)
	≥3	0 (0)	0 (0)	0 (0)	0 (0)
	Total	81 (0)	99 (4)	7 (0)	187 (4)

zero (2.9%), a normal Marquette ECG (2.1%), and an MMI of <15% (0.7%). Forty patients (7.5%) had a borderline ECG, 286 (55.8%) had an abnormal ECG, and 187 (36.5%) a normal ECG. There was no statistical difference between the 100 day mortality of patients with borderline and abnormal ECGs (i.e. 7.5% versus 9.1%).

No patients had a Tan ECG score over 6 and the mortality rate for the 71 (14%) patients with a score between 3 and 6 ranged from 15% to 20% (Figure 1). The 140 (27.3%) patients with a Tan ECG score of 1 and the 63 (12.3%) patients with a Tan score of 2 had statistically similar mortality rates to the 239 (46.6%) patient with a score of zero (i.e. 7.1%, 6.3% and 2.9%, respectively). There was a linear association between 100 day mortality and MMI values. Of the 139 (27.3%) patients with an MMI below 15% only one (0.7%) died. Over half the patients (52.6%) had an MMI between 15 and 24%, and 16 (5.9%) of them died (Figure 1).

Of the 187 (86%) patients with a normal ECG, 161 had a Tan score of zero and 81 (43%) had an MMI <15%; of the 239 (41%) patients with a Tan score of zero, 97 had an MMI <15%; 78 of the 329 (24%) patients with an abnormal or borderline ECG had a Tan score of zero and 60 (18%) had an MMI <15% (Table 3).

Logistic regression showed that, of the three ECG methods, only ECG-DM predicted 100 day mortality independently of the patient's age. Since both age and the MMI had similar odds ratios (i.e. 1.10 (95%CI 1.05 – 1.14) and 1.03 (95% CI 1.00 – 1.05)), they could be simply combined to make a MMI plus age score that had a Homer-Lemshow statistic for goodness-of-fit of 0.37. This MMI plus age score had a linear correlation with 100 day mortality: no patients with a MMI plus age score <85 died (Figure 1).

There was no statistical difference in c statistics for ECGs interpreted by Marquette, the Tan score and MMI, which were 0.636 (SE 0.054), 0.681 (SE 0.053) and 0.725 (SE 0.051), respectively. However,

the MMI plus age score had a c statistic of 0.807 (SE 0.047), which was statistically higher than the c statistic for Marquette ECG interpretation (p 0.015).

With the exception of borderline versus normal ECG and a Tan score of 1-2 versus zero, the odds ratio and risk differences of different values for each ECG method were all statistically significant (Table 4). There were no significant differences in the following Kaplan-Meier survival curve comparisons: a normal ECG, a Tan score of zero, MMI <15% and MMI plus age of ≤80; a borderline ECG, a Tan score 1-2, MMI 15-24% and MMI plus age 81-100; an abnormal ECG, a Tan score ≥3, MMI ≥25% and MMI plus age >100.

There was a significant difference between the Kaplan-Meier survival curves for normal and abnormal ECGs (p 0.003), but not between normal and borderline (p 0.08) and borderline and abnormal ECGs (p 0.74). The difference between the survival curves of patients with a Tan ECG score of zero and those with a score of 1-2 just failed to reach statistical significance (p 0.053), but was significant between a score of 1-2 and a score ≥3 (p 0.01). The survival curves for different levels of MMI and MMI plus age were all statistically different (Figure 2).

Discussion

This study shows that prediction of 100 day mortality by Marquette proprietary ECG interpretation software, the Tan ECG score and ECG-DM are equivalent. However, it is probable that if more patients had been studied the differences between both Marquette interpretation and the Tan score with ECG-DM would have reached statistical significance. Unlike previous reports we did not find the predictions of mortality by Marquette ECG interpretations or the Tan score to be independent of age.

This unfunded study only examined a convenient sample rather than consecutive patients. It is also

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Table 4. Mortality, odds ratio and risk differences according to Marquette ECG interpretation, Tan score, MMI and MMI plus age score

	Percent of patients	Alive	Dead	100 day Mortality (%)	Odds ratio (95% CI)	Chi-square	P	Risk difference (95% CI)	Fisher exact P
Marquette ECG									
Normal	36.5%	183	4	2.1%	-	-	-	-	-
Borderline	7.8%	37	3	7.5%	3.71 (0.80 - 17.27)	1.63	0.20	5.4% (-3.1 - 13.8%)	0.11
Abnormal	55.8%	260	26	9.1%	4.58 (1.57 - 13.33)	8.07	0.005	7.0% (3.0 - 10.9%)	0.002
Tan ECG score									
0	46.5%	232	7	2.9%	-	-	-	-	-
1-2	39.6%	189	14	6.9%	2.46 (1.00 - 6.21)	3.00	0.08	4.0% (-0.1 - 8.1%)	0.07
>=3	13.8%	59	12	16.9%	6.74 (2.54 - 17.87)	16.23	0.00006	14.0% (5.0 - 22.9%)	0.0001
MMI (%)									
<15%	27.3%	139	1	0.7%	-	-	-	-	-
15-24%	52.6%	254	16	5.9%	8.76 (1.15 - 66.73)	5.06	0.02	5.2% (2.1 - 8.4%)	0.009
>=25%	20.1%	87	16	15.5%	25.56 (3.33 - 196.21)	17.82	0.00002	14.8% (7.7 - 22.0%)	<0.00001
MMI plus age									
<=80	36.0%	186	0	0.0%	Undefined	-	-	-	-
81-100	35.9%	175	9	4.9%	Undefined	7.38	0.007	4.9% (1.8 - 8.0%)	0.002
>100	28.1%	119	24	16.8%	Undefined	31.23	<0.0001	16.8% (10.7 - 22.9%)	<0.0001

flawed by its small size and by Tan et al's score being determined by only one person, albeit blinded at the time to the identity and outcome of the patient. Use of the Tan score frees ECG prognostication from the need to use proprietary software. However, the score failed to show a consistent linear increase in mortality risk, and only showed a statistically significant increase in mortality in the 14% of patients who had a score >=3. In contrast, MMI and MMI plus age showed a consistent linear increase in mortality that was statistically significant on Kaplan-Meier survival curves.

The mortality rate of patients admitted to our hospital has fallen since its service was reconfigured in 2010, and this study only examined 30% of the patients admitted through the hospital's MAU. In our study performed between 2000 and 2005 the 30-day mortality rate was 4.7% compared with 2.3% in this study. Nevertheless there was no statistical difference between the odds ratio for 30 day mortality for an ECG interpreted as normal by Marquette software in these populations (i.e. odds ratio 0.19 (95%CI 0.14 - 0.27) versus 0.18 (95%CI 0.04 - 0.74).

ECG-DM offers several advantages over the traditional 12 lead ECG. The device currently costs approximately £5000, it can be quickly applied, it takes only 30 seconds to perform, and requires little skill or training to interpret. Only one (0.7%) of the patients with an MMI <15% died - he was 79 years of age and had a Charlson co-morbidity index of 7. All of the four patients with a normal ECG who died had MMI values of 15-24%. The MMI reflects abnormalities in the myocardium at a metabolic level, which may include ischemia and other causes. ECG-DM changes, therefore, are not diagnostic of any specific cardiac disease but are nonspecific indicators of myocardial health.¹³

Prognostication has been recognized as an important but often neglected part of patient management.¹⁶ The MMI plus age score's c-statistic of 0.812 and Homer-Lemshow statistic of 0.20 shows it has excellent discrimination and goodness-of-fit. Acute hospitalization, especially of the elderly, is an opportunity to recognize patients at risk of imminent decline and mortality and make appropriate arrangements in keeping with their wishes.¹⁸ This study suggests that some of these

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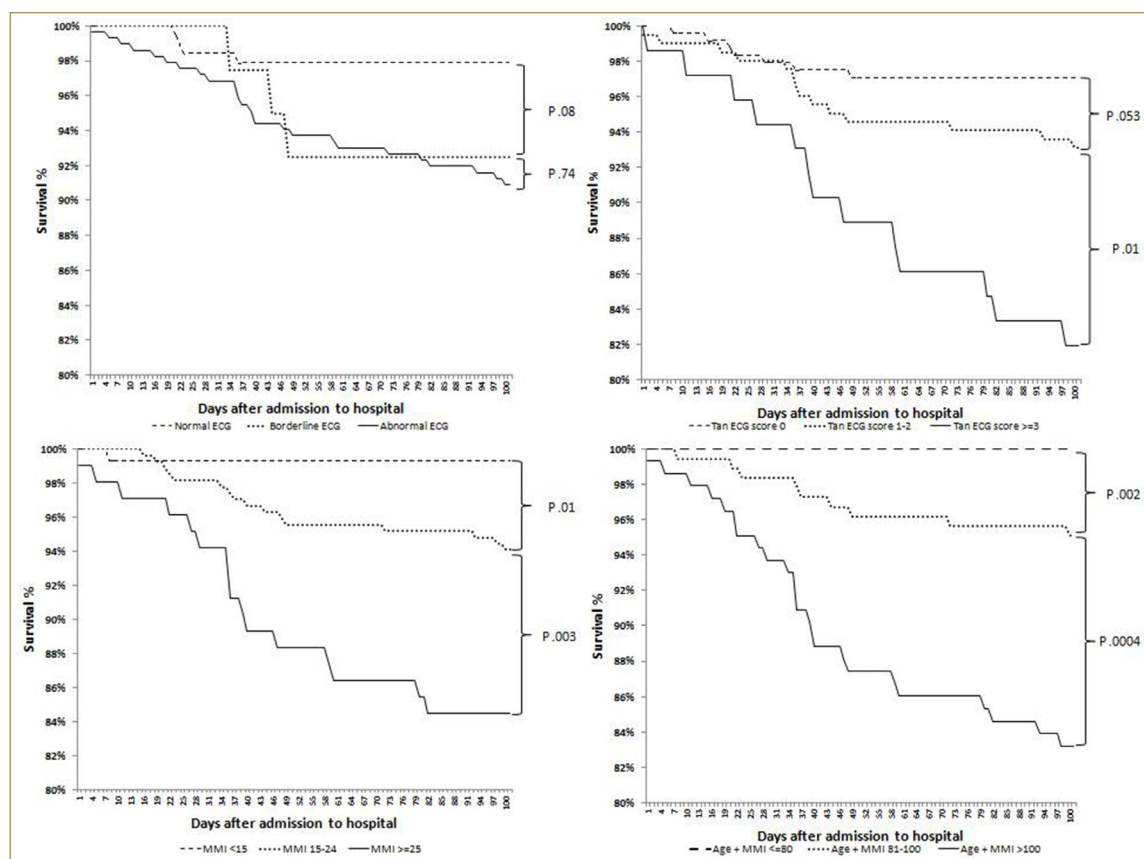


Figure 2. Kaplan Meir survival curves of different Marquette ECG interpretations, the Tan ECG score, and MMI and MMI plus age score.

patients might be more cheaply, rapidly and easily identified at the bedside by simply combining their MMI score with their age.

Why this study is important for Acute Physicians?

One of the main reasons patients get admitted to hospital is the fear that they may die.

An abnormal ECG is surprisingly a powerful predictor of mortality in acutely ill medical patients

This study shows that a non-proprietary scoring system that any doctor can perform at the bedside determines ECG abnormality as well as Marquette proprietary software

A novel and simple ECG technology is introduced that may be of value in the routine assessment of acutely ill medical patients

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Conflict of interest statement

This study was funded entirely by the authors and they have no conflict of interest with any third party.

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