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THE PROGNOSTIC VALUE OF NEW LEFT BUNDLE BRANCH BLOCK IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS.

by

BELAL MOHAMMAD AL RAJOUB

A project

submitted in partial fulfillment of the requirements

for the degree of Master of Science in Nursing, Adult care track

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of the Faculty of Medicine

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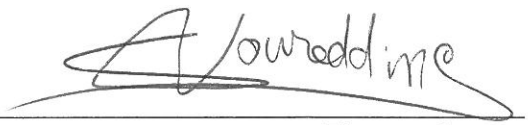

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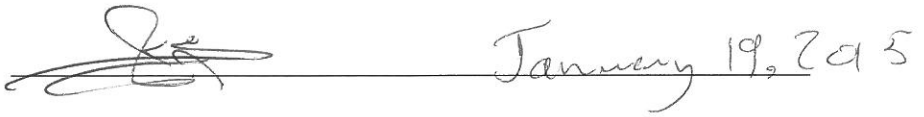

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AN ABSTRACT OF THE PROJECT OF

Belal Mohammad Alrajoub for Master of Science
Major: Nursing

Title: The Prognostic Value Of New Left Bundle Branch Block In Patients With Acute Myocardial Infarction: A Systematic Review And Meta-Analysis.

Background: Bundle branch block (BBB) is a conduction disorder that affects one or both branches of the bundle of His. Several factors were found to be associated with the development of BBB including acute myocardial infarction (AMI). Contradictory data exist concerning the independent contribution of left BBB to the risk of death among patients with AMI.

Objective: To assess the prognostic value of new LBBB in patients who present with AMI.

Methods: A systematic search of Medline, PubMed, CINAHL, and EMBASE was conducted without using any restrictions. Screening of the retrieved citations was made independently and in duplicate by the main investigator and five team members. Inverse variance meta- analysis was performed and summary effects presented as odds ratios and confidence intervals. Summary effects were presented for adjusted effect estimates when available; otherwise adjusted and unadjusted effect estimates were pooled. The I2 statistic was used to assess heterogeneity. Assessment of risk of bias was made by two authors independently.

Results: The included eight eligible studies involved a total of 105,861 participants. New LBBB was associated with a statistically significant risk of mortality at 30 days (OR: 2.10, 95% CI 1.27 to 3.48; I2: 85%) and one year follow up (OR: 2.81, 95% CI 1.64 to 4.80; I2: 4%). Also, new LBBB was associated with a statistically significant increase in the risk of development of congestive heart failure (OR: 2.64, 95 % CI: 1.84 to 3.77; I2: 79% .(

Conclusion: New LBBB is associated with higher risk of mortality both at 30 days and one year follow up, and a higher risk of developing congestive heart failure. However, these results should be interpreted with caution due to the small number of studies and risk of bias in some of studies. More research is needed on this topic.

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ABBREVIATIONS

MI: Myocardial Infarction.

AMI: Acute Myocardial infarction.

BBB: Bundle Branch Block.

LBBB: Left Bundle Branch Block.

RBBB: Right Bundle Branch Block.

ACC: American College of Cardiology.

AHA: American Heart Association.

ESC: European Society of Cardiology.

ACS: Acute Coronary Syndrome.

CHAPTER I

Background

Bundle branch block (BBB) is a conduction disorder that affects one or both branches of the bundle of His. The block may be complete, or incomplete, such as conduction blocks that affect one of the fascicles of the left bundle branch (anterior or posterior). Many factors are associated with the development of BBB, including valvular heart diseases, hypertension, cardiomyopathies, myocarditis, and coronary artery disease including acute myocardial infarction (AMI) (Imanishi et al., 2006). If untreated, BBB may progress to a complete atrio-ventricular (AV) block, bradyarrhythmias and other serious adverse outcomes including sudden cardiac death, torsades de pointes and ventricular escape rhythms (Moser & Riegel, 2008 .(

In the general population, the prevalence of BBB (right and left) was found to be higher in males and age- dependent. Right bundle branch block (RBBB) was found to be twice as frequent in males than in females, with a prevalence ranging from 0.6% in females under age 40 years to 14.3% in males older than 80 years (Bussink et al., 2013). Similarly the prevalence of left bundle branch block (LBBB) was reported to range from 1% in middle age to around 17% in the older population (Gunnarsson, Eriksson, & Dellborg, 2000).

Many studies have shown that patients with BBB that accompanies an acute episode of MI may experience a worse prognostic profile than AMI patients who present with normal conduction (Bhalli, Khan, Samore, & Mehreen, 2009; Cleempoel et al., 1986; Jim, Chan, Tse, & Lau, 2009; Terkelsen et al., 2005; Ting et al., 2007). Currently, there is a group of researchers working on a systematic review and meta- analysis that examined the prognostic value of RBBB in the context of acute coronary syndrome

(ACS); they concluded, in the published abstract of this study, that patients with RBBB and AMI are at more than 2-fold higher risk of all-cause mortality at 30 days follow up (Hazem et al., 2014); however, in this abstract there was no information available regarding the onset of the RBBB, whether new or old. Wong et al, (2006) reported that patients with RBBB demonstrated a higher 30- day mortality regardless of the onset of the disease (Adjusted odds ratio [OR] for old RBBB: 2.48, 95% confidence interval (CI) 1.93–3.19; adjusted OR for new RBBB: 3.84, 95% CI 2.38–6.22).

To date, there is no consensus on the independent contribution of LBBB in cause specific mortality in patients with AMI. Many cohort studies reported that LBBB is associated with and may be an independent predictor of higher mortality rates among patients with AMI (Barron, Rundle, Ornato, & Avins, 1998; Guerrero et al., 2005; Brilakis et al., 2001; Go, Jain & Mehta, 2003; Kleemann et al., 2008; Kontos et al., 2011; Sgarbossa et al., 1998; Sorensen et al., 2013). On the other hand, many other studies reported that LBBB is not an independent predictor of mortality in this group of patients, and higher mortality rates in this population can be explained by their higher baseline risk due to several risk factors (Brembilla-Perrot et al., 2008; Nazif et al., 2014; Stenestrand et al., 2004; Yeo et al., 2012). Moreover, the majority of the published studies did not differentiate between old and new onset LBBB (nLBBB). Often studies of nLBBB include patients who have evidence of AMI or new or presumed new LBBB. It is important to note that diagnosis of MI is highly challenging in the presence of LBBB. Evidence of AMI includes ischemic chest pain lasts more than 20 minutes, positive cardiac enzymes (CK-MB and Troponin) and ECG signs including ST segment elevation of >=1 mm in 2 or more limb leads, or >= 2 mm in 2 or more contiguous precordial leads, ST depression MI or new or presumed

new LBBB . The current guidelines (2013) from the American College of Cardiology/ American Heart Association (ACC/AHA) recommend to use a specific diagnostic criteria that were developed by Sgarbossa et al. (1996); scores are given based on 3 criteria; ST-elevation of at least 1 mm that is concordant with the QRS complex (5 points), ST-segment depression of at least 1 mm in lead V1, V2, or V3 (3 points), and ST-elevation of at least 5 mm that was discordant with the QRS complex (2 points). Score of ≥ 3 has a specificity of 98% for acute myocardial infarction, but a score of 0 may not rule out STEMI (O'Gara et al., 2013).

Wong et al. (2006) conducted a study to assess the prognostic differences between patients with different types of BBB in the context of AMI; they found that mortality within 30 days is almost 3 times higher in patients with definite nLBBB compared to patients with normal conduction (Unadjusted OR: 4.68, 95% CI: 2.02 to 10.87; adjusted OR: 2.97, 95% CI: 1.16 to 7.57). The researchers also included 300 patients with LBBB that was present on ECG at baseline, and grouped those patients as presumed new LBBB. However, there was no real association with mortality in this group (Unadjusted OR: 1.90, 95% CI1.39 to 2.59; adjusted OR for baseline characteristics OR:1.10, 95% CI: 0.79 to1.53; and when analysis further adjusted for presented features of AMI, OR was reduced to 0.69, 95% CI: 0.48 to 0.99). This finding highlights the importance of accurate identification of the onset of the LBBB. In addition, many other research studies reported that patients with nLBBB are at higher risk of in-hospital and one year mortality, heart failure, and high degree AV block when compared to patients without this conduction abnormality (Al-Faleh et al., 2006; Azadani et al., 2012; Brown et al., 2013; Miller et al., 2001; Widimsky et al., 2012). To the best of our knowledge, there is no systematic review of the prognostic value of new or presumed new LBBB in patients with AMI.

Since patients with nLBBB are considered a high risk group, and could benefit from early reperfusion therapies, the current guidelines from ACC/AHA (2013) and the European Society of Cardiology (ESC) recommend that patients with acute coronary syndrome who present with new or presumed new left BBB be considered for early reperfusion therapy using percutaneous coronary intervention (PCI) or fibrinolytic therapy (O'Gara et al., 2013; Steg et al., 2012), However, several researchers reported that this recommendation was based on studies performed several years ago and the population subgroups of those studies may differ substantially from the contemporary population considering the current advancements in management strategies particularly after the era of percutaneous coronary intervention (PCI) (Brown et al., 2013; Neeland, Kontos, & de Lemos, 2012). For example the introduction of thrombolytic therapy and PCI in the 1980s has led to a significant reduction in mortality in patients with AMI (National Heart Attack Alert Program Coordinating Committee, 1994), thus recommendations may need to be revisited based on more recent studies .

A recent study that reviewed the National Cardiovascular Data Registry (NCDR) and Acute Coronary Treatment and Intervention Outcomes Network (ACTION) Registry–Get With the Guidelines (GWTG) included 46,006 patients from 333 sites; the authors found that only 48.3% of eligible patients with LBBB received emergent reperfusion therapy (thrombolysis or PCI), which suggests non- adherence to the AHA and ESC guidelines (Yeo et al., 2012). This non- adherence to the guidelines could be explained by the clinical challenges of diagnosing AMI in case of the presence of LBBB. Sgarbossa criteria may have limited clinical utility in certain circumstances due to low sensitivity (Jain et al., 2011). Moreover, in a recent cohort study of consecutive patients referred for PCI, the authors found that only 17.5% of

nLBBB referrals were appropriate, that is a thrombotic culprit lesion was identified by PCI, which suggests a low prevalence of AMI in this group of patients (Brown et al., 2013). Similarly, Chang et al, (2009) reported even a much lower prevalence (7.3%) of MI in patients with nLBBB who presented with ischemic symptoms to the emergency department. The large proportion of inappropriate referrals could be explained by under-estimating the risk associated with the presence of BBB in those patients because of the conflicting results in the literature. It also highlights the need for developing more rigorous diagnostic criteria.

This study aims to present a systematic review and meta-analysis on observational studies in order to assess the prognostic value of new left bundle branch block in hospitalized patients with AMI. The findings of this review will help fill the gap in knowledge in this area and provide a thorough analysis of the state-of-the science on the adverse effect of nLBBB in the context of AMI.

CHAPTER II

Methods

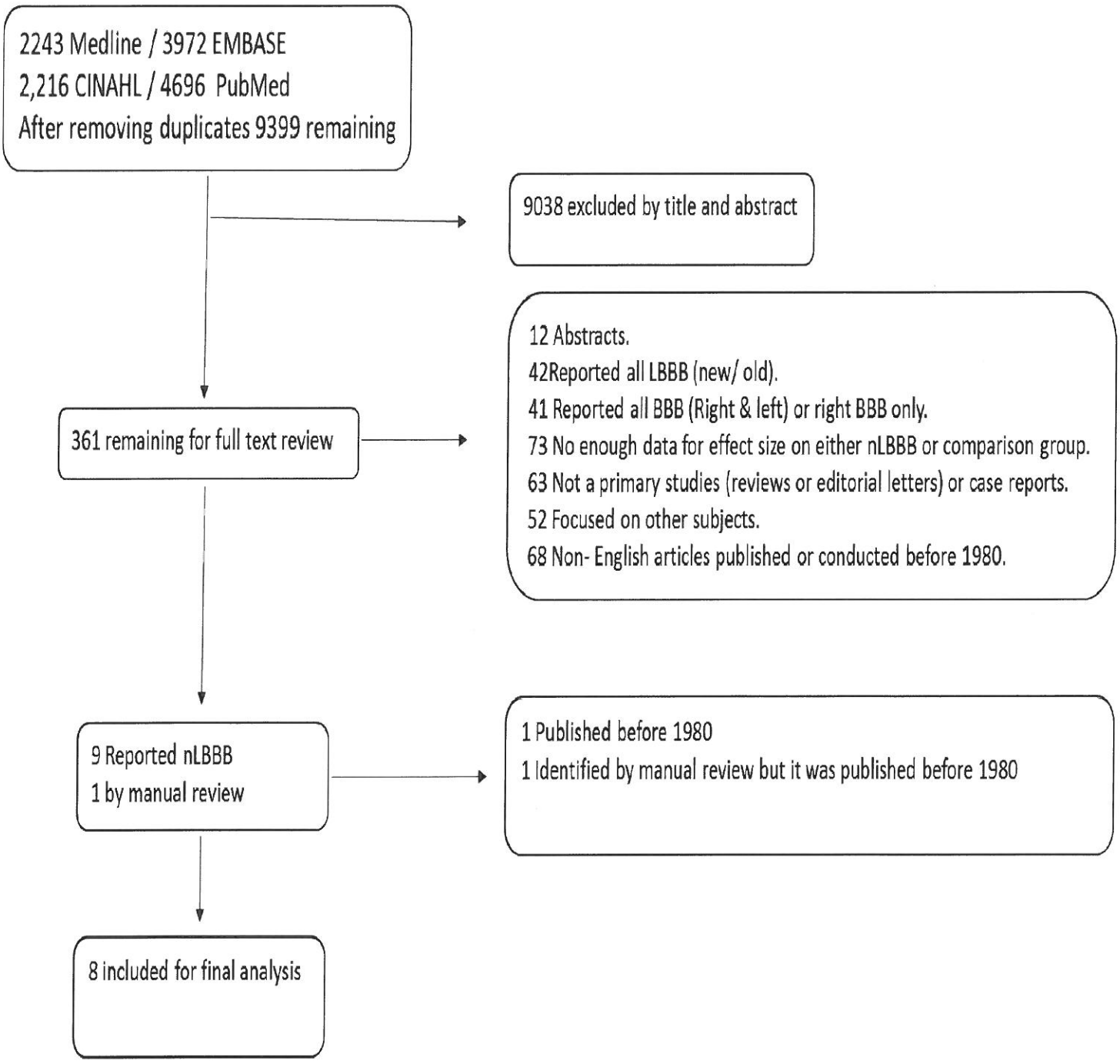
Search strategy and selection criteria.

A systematic search of PubMed, Medline, EMBASE, and CINAHL databases was made by using the following Medical Subject Headings: myocardial infarction, bundle branch block, prognosis, and survival analysis. The retrieved references were combined in one folder and duplicates were removed using RefWorks. The same procedure was repeated using EndNote software to ensure comprehensiveness and not missing any relevant reference. A manual search of references cited by the published original studies was also performed. No restrictions or limits were used in the search. For studies that were published in non-English languages, the online Google Translate feature was used for translation. Detailed search strategies for each database are shown in appendix 1. There were initially 9,399 references retrieved that were possibly relevant.

The protocol of this study was published on PROSPERO (registration number: CRD42014015286). The primary investigator (PI) screened all references, and five other team members screened the same references in duplicate and independently. The first round of screening included the titles and abstracts of a total of 9,399 references. Then once relevant references were identified, the full text articles were retrieved and a second round of screening was made by the primary investigator and the five team members in duplicate and independently. Inclusion criteria were: observational studies (cohort or case- control) that included patients with nLBBB and AMI and compared them to patients with AMI but without conduction abnormalities. The primary outcomes were in-hospital mortality (or mortality within 30 days); and

one year mortality. Secondary outcomes were congestive heart failure (CHF), atrioventricular block (AV block) that developed after LBBB, and placement of pacemaker. since bradydysrhythmias were a consequence of BBB that may be treated with pacemaker therapy. Studies that reported adjusted and unadjusted risk estimates were included. Upon reviewing the literature, it became clear that the date of the research is an important consideration in selecting studies for this meta-analysis. The use of revascularization, namely PCI and thrombolytic therapy, which became the PI available in the 1980s, has reduced mortality rates significantly in AMI patients (National Heart Attack Alert Program Coordinating Committee, 1994). Provision of thrombolytic treatment within one hour of MI was associated with 50% reduction in mortality; at 3 hours, a 25% reduction was noted. Thus including studies done before and after this era would introduce a significant bias since the current study is examining the prognostic value of LBBB in AMI patients, including the risk for mortality. Thus a decision was made to exclude studies conducted prior to 1980. The inclusion criteria were communicated to the team members along with the data extraction sheet then after the second round of screening met with the team members to double check results of screening. Differences were resolved but no major disagreements were noted. The Study flow is depicted in figure 1 .

Figure 1. Study Flow



Data extraction.

Data was extracted by two authors (Alrajoub and Noureddine) independently. A standardized form was used for this purpose (appendix 2). Discrepancies were solvedby verbal discussion and going back to the articles; again here no major disagreements were noted. Study characteristics that were recorded were as follows:

surname of first author; year of publication; study design and funding source if available; country of origin; description of participants; exposure group; comparison group; data for outcome measurement; calculated effect sizes or raw data for in-hospital mortality; one year mortality; development of CHF; AV block; and placement of pacemaker. Study quality and risk of bias were assessed based on the appropriate development of sample inclusion and exclusion criteria; exposure measurement; outcome measurement; controlling for confounding; and completeness of data. Adjusted and unadjusted estimates were extracted and reported for each outcome separately.

Statistical Analysis.

Effect sizes are presented as odds ratios (OR) with the corresponding confidence interval (CI) because most of the included studies either reported effect sizes as odds ratios, or reported data from which it was possible to calculate OR and the corresponding CI. Data synthesis was based on an inverse variance meta- analysis. Effect sizes were combined using the random effect model to generate the summary effect size. Forest plots were used to express the effect size data of each study and summary OR (with 95% CI) estimated for one year mortality, 30 days mortality and CHF. It is worth noting that none of the studies reported AV block or pacemaker data. Separate meta- analysis was also conducted on studies that reported adjusted 30 days mortality by following the same procedure described previously. The analysis was performed using REVMAN version 5.3. Heterogeneity between the included studies was assessed by using the I-squared statistic. We considered an I-squared value greater than 50% as indicative of substantial heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003).

CHAPTER III

Results.

Studies and participants characteristics are presented in table 1. Of 9,399 citations included for title and abstract screening, 9,038 were excluded as noted in figure 1. The remaining 361 citations were included for full text screening. Only 8 observational cohort articles met the inclusion criteria. One of the included studies was published in Serbian language; the remaining articles were published in English. Studies that were conducted before 1980 and published in non-English were not screened as full text (68 articles). Among the studies that were published in English before 1980, only two studies reported data on nLBBB. Study flow and reasons for exclusion are depicted in figure 1. Of the eight included studies; two were conducted in the USA; two were multicenter studies conducted in many countries; one in Czech Republic; one in Serbia; one in the UK; and one in Mexico. The total sample sizes ranged from 577 in the study by Mijailovic et al (2008) to 46,006 in the study by Yeo, et al (2012). The total number of participants in all the studies combined was 105,861 .

Two studies included consecutive patients admitted to coronary care unit (Mijailovic et al.; 2008, Miller et al., 2001) ; one study included consecutive patients referred for coronary angiography (Widimsky et al., 2012); one study included consecutive patients referred for PCI (Brown et al., 2013); two studies retrieved their data from national cardiology registries (Juarez-Herrera et al., 2010; Yeo, et al., 2012); the remaining two studies were a secondary analysis of the databases of randomized controlled trials (Al-Faleh et al., 2006; Wong., et al, 2006 .(

Two studies reported one year mortality: Al-Faleh et al. (2006) reported adjusted OR (adjusted for baseline characteristics), while Brown et al. (2013) reported raw data for one year mortality. Seven out of eight studies reported in-hospital mortality (or mortality within 30 days); however, two of those articles failed to adjust for confounding (Mijailovic et al. 2008; Widimsky et al., 2012). Two studies reported data on CHF (Al-Faleh et al, 2006; Yeo et al., 2012). None of the included studies reported data on AV block or placement of pacemaker.

Table 1: Characteristics of Included Studies

Study Name	Study design/ funding	Sample size	Participants	Exposure	Comparison	Outcomes	Country
Miller et al. (2001)	Cohort. Funding N.R.	907	Patients admitted to CCU with AMI	Patients with AMI and new LBBB	Patients with AMI and normal conduction	In-hospital mortality	USA
Widimsky et al. (2012)	Cohort. Partially supported by the Charles University Prague research project.	6,742	Consecutive patients with AMI who underwent coronary angiography	Patients with AMI and new LBBB	Patients with AMI and normal conduction.	In-hospital mortality	Czech Republic
Wong et al. (2006)	Cohort. The author H.D.W. received partial support from the Green Lane Research and Educational Fund Board	15,365	Secondary analysis of HERO- 2 trial data	Patients with AMI and new LBBB	Patients with AMI and normal conduction	In-hospital mortality	International (46 countries)
Yeo et al. (2012)	Cohort. Multiple funding sources for different authors	46,006	Data from the ACTION-GWTG registry	Patients with AMI and New LBBB	Patients with STEMI without LBBB	In-hospital mortality CHF	USA
Mijailovic et al. (2008)	Cohort. Funding N.R	577	Consecutive patients admitted to CCU with AMI	Patients with AMI and new LBBB	Patients with AMI and normal conduction	In-hospital mortality	Serbia
Brown et al. (2013)	Cohort. Funding N.R.	1,445	Patients presenting for PPCI at one tertiary referral	Patients with AMI and new LBBB	Patients with STEMI without LBBB	One year mortality	UK

			center				
Al-Faleh et al (2006)	Cohort. Funding N.R.	22,839	Data from 2 trials (ASSENT 2 and 3 trials)	Patients with AMI and new LBBB	Patients with AMI and normal conduction	In- hospital and one year mortality, HF	International (29 countries)
Juarez-Herrera et al (2010)	Cohort. Funding N.R.	4,237	Data from registry of the Mexican Cardiology Society	Subgroup of patients with AMI and new LBBB	Patients with AMI and normal conduction	In-hospital mortality	Mexico
		Total: 105,861					

Legend: N.R.: Not reported. ACTION-GWTG: National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines; AMI: Acute Myocardial Infarction. LBBB: Left Bundle Branch Block. STEMI: ST- Elevation Myocardial Infarction. CHF: Congestive Heart Failure. UK: United Kingdom.

Figure 2 shows the results of meta- analysis for one year mortality. New LBBB was associated with almost 3-fold higher risk of all-cause mortality in the first year of follow up (OR: 2.81, 95% CI: 1.64 to 4.80). Similarly, as noted in figure 3, nLBBB found to be significantly associated with 30 days mortality (OR: 2.10 95% CI: 1.27 to 3.48). For 30 days mortality, the analysis was based on pooled adjusted and unadjusted effect sizes. As shown in figure 4, nLBBB was significantly associated with increased risk of mortality within 30 days even when the studies that reported unadjusted effect estimates were excluded (OR: 1.73 95% CI: 1.04 to 2.88; I^2:79%).New LBBB was also associated with a statistically significant increase in the risk of developing CHF (OR: 2.64 95 % CI: 1.84 to 3.77; I^2: 79%) as noted in figure 5.

Figure 2. One year mortality

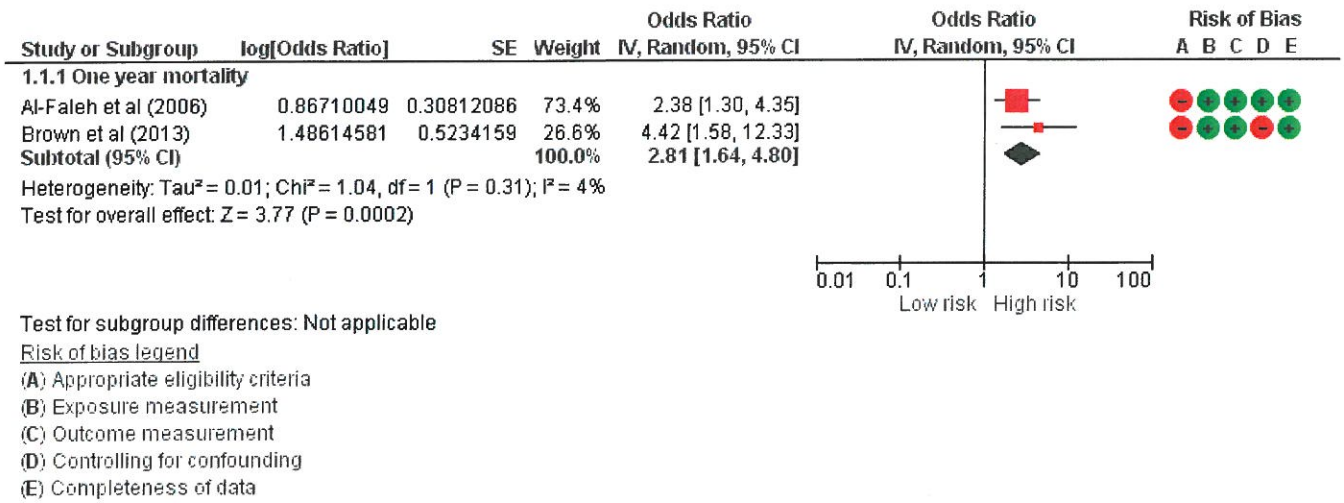
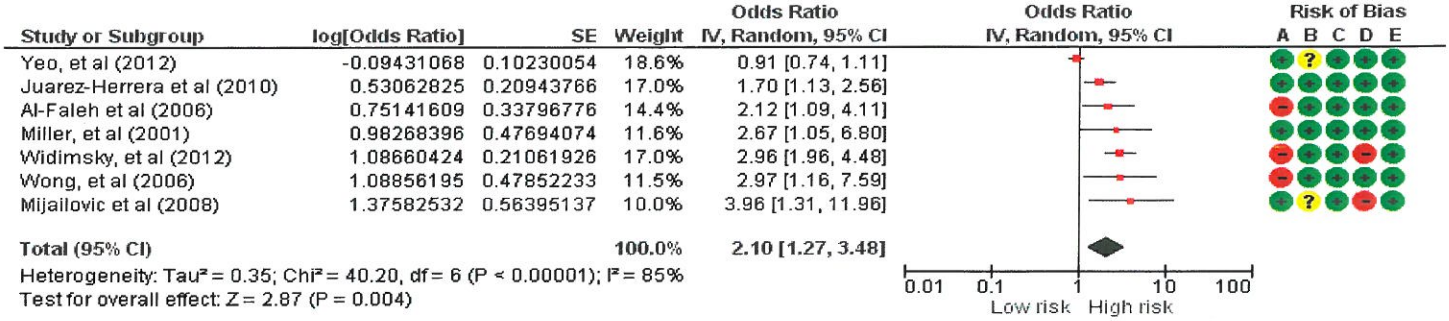
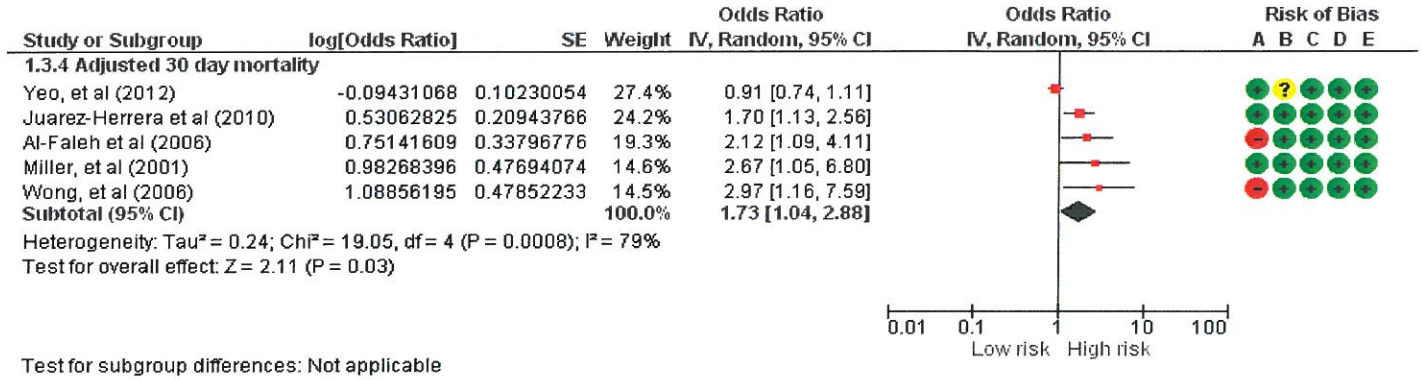


Figure 3. Mortality at 30



Risk of bias legend
(A) Appropriate eligibility criteria
(B) Exposure measurement
(C) Outcome measurement
(D) Controlling for confounding
(E) Completeness of data

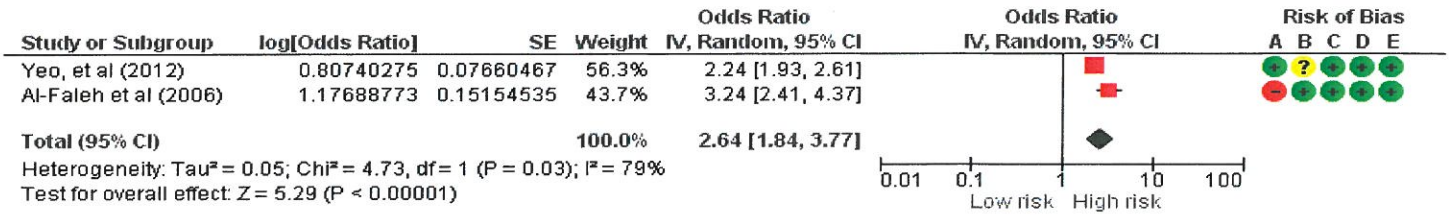
Figure 4. Adjusted 30 days mortality.



Test for subgroup differences: Not applicable

Risk of bias legend
(A) Appropriate eligibility criteria
(B) Exposure measurement
(C) Outcome measurement
(D) Controlling for confounding
(E) Completeness of data

Figure 5. Congestive Heart Failure.



Risk of bias legend
(A) Appropriate eligibility criteria
(B) Exposure measurement
(C) Outcome measurement
(D) Controlling for confounding
(E) Completeness of data

As mentioned previously, Wong et al. (2006) included 300 patients with LBBB that was present on ECG at baseline, and grouped those patients as presumed new LBBB. When the effect estimate of this group was included in the meta- analysis of adjusted 30 days mortality instead of the effect estimate of the group of 25 patients that was defined as definitely new LBBB as they showed new LBBB within 60 minutes of starting their thrombolytic therapy, the summary effect was in the same direction, but it failed to show statistical significance (OR: 1.28, 95% CI: 0.84 to 1.97; I2: 80%). Considering that Wong et al. (2006) used the same reference group to calculate effect estimates for definitely new LBBB and presumed new LBBB, and since we were searching for the best available evidence, we sought to use the effect estimate calculated for definitely new LBBB in the main analysis.

Substantial heterogeneity was found between the studies that reported 30 days mortality and those that reported information on CHF (I2: 87%, and I2: 79% respectively). Even after adjusting for confounders, and having the effects for 30-days mortality pooled, the test of heterogeneity remained significant (I2: 79%). In contrast, the test of heterogeneity for studies that reported one year mortality showed no significant heterogeneity (I2: 4%).

Assessment for risk of bias was made by two authors (Alrajoub and Noureddine) in duplicate and independently and discrepancies were solved by discussion. The results of assessment of risk of bias for each of the included studies and overall risk of bias in all studies are shown in figures six and seven respectively. The main biases were in the sample eligibility in half the studies and the lack of adjustment for confounding in three studies. Assessment of publication bias was not done due to small number of studies.

Figure 6. Assessment of risk of bias.

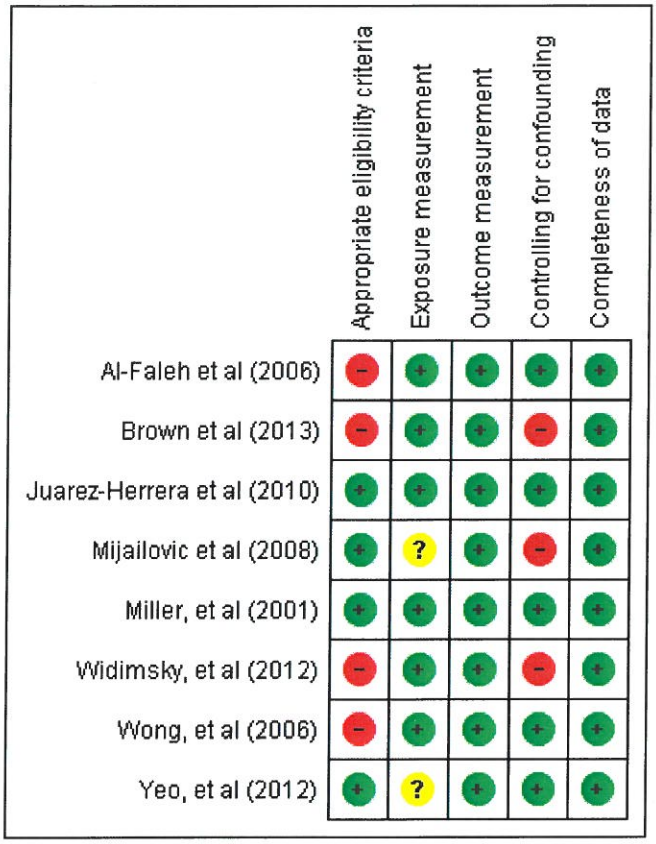
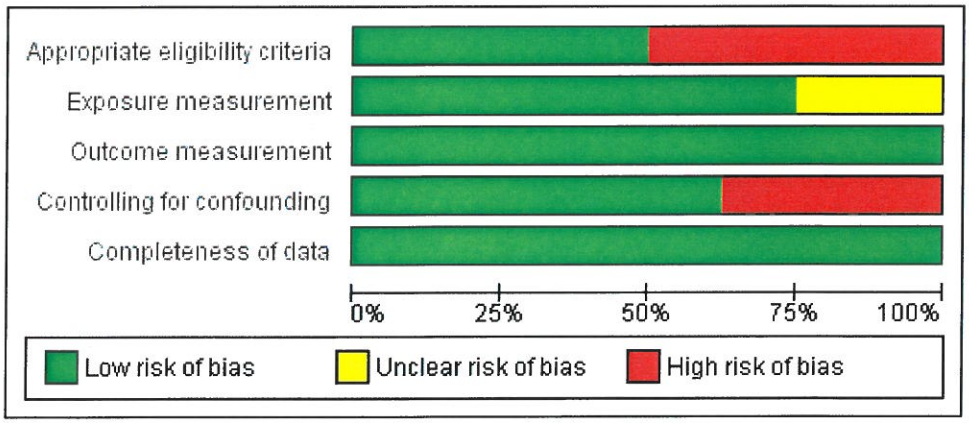


Figure 7. Overall risk of bias.



CHAPTER IV

Discussion.

This is the first meta- analysis of observational studies on the prognostic value of new LBBB in the context of AMI. Analysis was made for eight studies that involved a total of 105,861 patients. The results have shown that patients who present with nLBBB and AMI have an increased risk of 30 days, one year mortality and an increased risk of developing CHF. However, considering the small number of studies and the substantial heterogeneity, these results should be interpreted with caution.

There were only two studies that reported information on one year mortality. Al-Faleh et al, (2006) reported an adjusted effect estimate (OR: 2.38, 95% CI 1.30-4.35), adjustment was made for baseline characteristics that included but were not limited to age, gender, history of hypertension, diabetes mellitus, prior MI, PCI or coronary artery bypass graft (CABG), history of smoking, Killip class and other factors. However, this study included a select group of patients (analysis was made on data retrieved from two trials ASSENT- 2 (Van de Werf, 1999) and ASSENT- 3 (Wallentin et al., 2003). In both trials patients were treated with either tenecteplase or alteplase along with other adjunctive therapies; thus these samples were restricted to patients eligible for thrombolytic therapy. Brown et al, (2013) included consecutive patients referred for PPCI at a single tertiary referral center; moreover the authors failed to adjust for confounding. Considering the risk of selection bias in both studies and risk of confounding bias in the latter one, the summary effect may not be reliable even there was a statistically significant increase in risk of one year mortality and no substantial heterogeneity between those studies (OR: 2.81 95% CI 1.64 to 4.80; I2: 4%).

Information on 30 days mortality was provided by seven out of eight studies. Wong et al. (2006) conducted an analysis on data retrieved from the HERO-2 trial (White & Hirulog and Early Reperfusion or Occlusion (HERO)-2 Trial Investigators, 2001). Patients in this trial received streptokinase and aspirin and randomized to receive either bivalirudin or unfractionated heparin, again using a select patient group eligible for thrombolytic therapy. ECGs were performed at randomization and at 60 min after receiving fibrinolytic therapy. There were 300 patients presented with LBBB at randomization (presumed new LBBB), and another 25 patients developed LBBB after 60 minutes of receiving the fibrinolytic therapy. Data on patients with LBBB was presented separately for both groups (definitely new and presumed new LBBB). Two separate meta- analyses were conducted using effect estimates from the first and second group (300 with presumed new LBBB, and 25 definitely new LBBB). When adjusted and unadjusted effect estimates were pooled, by using estimate provided on the presumed new LBBB, there was a statistically significant increase in mortality, however, there was a substantial heterogeneity between the included studies (OR: 1.68, 95% CI 1.04 to 2.71; I2: 87%). A similar result was found when the effect estimate provided on 25 definitely new LBBB was used (OR: 2.10, 95% CI 1.27 to 3.48; I2: 87%). Meta- analysis on five studies that reported adjusted effect estimates was performed separately. When the effect estimate provided by Wong et al, (2006) for 25 definitely new LBBB was used, there was a statistically significant increase in mortality, however there was a substantial heterogeneity between the included studies (OR: 1.73, 95% CI 1.04 to 2.88; I2: 79%). In contrast, when the effect estimate provided by Wong et al, (2006) for 300 presumed new LBBB was used, the summary effect failed to show statistical significance (OR: 1.28, 95% CI 0.84 to 1.97; I2: 80%); however, it remained in the same direction in either case. This variation in the

summary effect may reflect the importance of the onset of the condition, where new onset LBBB was found to be associated with a significant increase in mortality as mentioned previously. Some researchers used previous ECGs to decide on the onset of the LBBB, and they considered the condition as new if previous ECGs showed no signs of LBBB; however this is not the case in all of the included studies, introducing a bias in the measurement of exposure as noted in the risk of bias analysis .

In general, heterogeneity between the included studies can be a result of many factors. The included studies involved patients from different settings, including select groups of patients in two studies. In addition, variation in the treatment modalities may have a substantial impact on the outcomes. The included studies were involving patients who underwent either PCI or received thrombolytic medications that included Streptokinase, Tenecteplase, and Alteplase. Some of the included studies did not even mention the treatment strategy that was followed in those patients. Moreover, the time from onset of symptoms to receipt of the treatment may have a substantial impact as well (Moser & Riegel, 2008). In few cases, the determination or criteria for LBBB were not clearly described. Some authors mentioned the criteria by Sgarbosa whereas others mentioned wide QRS and the shape of LBBB as diagnostic criteria.

Effect estimates of the risk of developing CHF were provided by two studies. There was a statistically significant increase in risk of CHF in patients with nLBBB, however there was again a substantial heterogeneity between the included studies (OR: 2.64 95% CI 1.84 to 3.77; I2: 79%). This summary effect may be misleading since both of those studies' investigators did not report the criteria that were followed to diagnose HF, or by whom the diagnosis was made. In addition, they did not account for other risk factors that may lead to the development of CHF, such as,

congenital heart defects, infections, some diabetes medications and alcohol consumption .

This analysis may have several limitations. There was a small number of studies that have met the inclusion criteria. In addition, the included studies were considerably variable with regards to the included participants and the treatment modalities that were used. Moreover, many of the included studies were prone to a high risk of bias, which may have a serious impact on the confidence in the summary effects. There is need for more rigorous studies with representative samples of the AMI population in general and more consistent control over relevant confounders .

Implications for Advanced Practice Nursing

Nurses are crucial participants in the management of patients with AMI. Particularly, nurses who work in the emergency department and those who work in the coronary care units should be aware of the substantial risk that may threaten the lives of patients who present with AMI and nLBBB. Nurses should be aware of high risk patients to be able to minimize the burden on patients' health and wellbeing. This particular group of patients should be considered as a high risk group and they should receive continuous and close monitoring. Advanced practice nurses (APNs) can mentor nurses working in coronary and emergency care in identifying LBBB and assessing patients accordingly.

This analysis represents a step in fulfillment of the research role of advanced practice nurses (APNs) where nurses should be involved in research conduction and creation of the evidence aiming for more advancement in health care. Cardiovascular APNs, in collaboration with cardiologists, can be instrumental in developing and maintaining a database of patients admitted with AMI, including risk factors, comorbidities,

treatments, LBBB and outcomes. Such databases will pave the way to conducting further studies in the field that will provide the best available body of evidence on this topic. Such studies are also helpful for managers and practitioners who aim to provide the best possible care for their patients in a timely and effective manner, leading to optimal patient outcomes. More importantly, this kind of research is helpful in risk stratification of AMI patients, which is a crucial role of bedside providers and has an impact of management decisions. Finally, such studies are also very helpful for nurse educators who aim to provide the best possible knowledge and learning experience for their students.

Conclusion

There was a statistically significant increase in mortality both at 30 days and one year in patients with new onset LBBB who present with AMI. In addition, patients who present with new onset LBBB in the context of AMI were found to be at higher risk of developing CHF when compared to patients with AMI and normal conduction. However, these results should be interpreted with caution due to several considerations including the small number of included studies and the risk of bias in many of the provided effect estimates. More research on this topic is needed. Future research should focus more on the actual onset of LBBB and other complications that may follow this kind of conduction abnormality such as AV block. One limitation to a definite diagnosis of new LBBB is lack of prior ECG; thus one recommendation is that at risk individuals ought to have baseline ECGs taken and documented. Moreover, future research should account for the variability in treatment modalities and variability in time to treatment in the analysis.

Appendix 1. search strategies for each data base.

Search strategy for CINAHL

#	Query	Results	Action
S1	(MH "Myocardial Infarction+") OR (MH "Myocardial Ischemia+") OR (MH "Infarction") OR (MH "Myocardial Reperfusion")	68,107	Edit
S4	(TI (heart* OR cardi* OR myocardi* OR coronar*) OR AB (heart* OR cardi* OR myocardi* OR coronar*)) N3 (TI (attack* OR infarct* OR shock* OR stun* OR hibernat* OR postinfarct* OR post-infarct* OR reinfarct* OR re-infarct* OR reperfus* OR re-perfus* OR ischemi* OR ischaemi* OR necros* OR thromb* OR occlus* OR atherosclero* OR block* OR obstruct* OR clos* OR plug* OR clog* OR plaqu* OR emboli* OR clot*) OR AB (attack* OR infarct* OR shock* OR stun* OR hibernat* OR postinfarct* OR post-infarct* OR reinfarct* OR re-infarct* OR reperfus* OR re-perfus* OR ischemi* OR ischaemi* OR necros* OR thromb* OR occlus* OR atherosclero* OR block* OR obstruct* OR clos* OR plug* OR clog* OR plaqu* OR emboli* OR clot*))	35,595	EditS4
S5	(TI Coronar* OR AB Coronar*) N3 (TI (syndrom* OR diseas* OR disorder*) OR AB (syndrom* OR diseas* OR disorder*))	21,601	EditS5
S6	(MH "Coronary Thrombosis") OR (MH "Coronary Arteriosclerosis") OR (MH "Coronary Stenosis+") OR (MH "Coronary Disease+") OR (MH "Coronary Vasospasm+") OR (MH "Acute Coronary Syndrome")	36,923	EditS6
S7	S1 OR S4 OR S5 OR S6	86,189	EditS7
S8	(MH "Bundle-Branch Block") OR (MH	1,517	EditS8

	"Bundle of HIS")		
S9	(TI (fascic* OR bundle* OR branch*) OR AB (fascic* OR bundle* OR branch*)) N3 (TI block* OR AB block*)	24,691	EditS9
S10	(MH "Purkinje Fibers")	147	EditS10
S11	(TI (Purkinje* OR kent* OR hiss OR his) OR AB (Purkinje* OR kent* OR hiss OR his)) N3 (TI (fiber* OR bundle* OR block*) OR AB (fiber* OR bundle* OR block*))	472	EditS11
S12	S8 OR S9 OR S10 OR S11	25,707	EditS12
S13	(MH "Prognosis+")	232,875	EditS13
S14	TI (prognos* OR surviv* OR futilit* OR mortalit* OR risk* OR hazard* OR forecast* OR fore-cast* OR foretell* OR fore-tell* OR determin* OR predict* OR comorbid* OR co-morbid* OR complicat*) OR AB (prognos* OR surviv* OR futilit* OR mortalit* OR risk* OR hazard* OR forecast* OR fore-cast* OR foretell* OR fore-tell* OR determin* OR predict* OR comorbid* OR co-morbid* OR complicat*)	675,416	EditS14
S15	(TI independ* OR AB independ*) N3 (TI (indicat* OR factor* OR influen* OR featur* OR caus* OR element* OR reason* OR contribut*) OR AB (indicat* OR factor* OR influen* OR featur* OR caus* OR element* OR reason* OR contribut*))	9,754	EditS15
S16	(TI (treat* OR interven* OR manage* OR admission* OR readmission* OR re-admission* OR hospitaliz* OR hospitalis* OR therap* OR relaps* OR remission* OR recurrent*) OR AB (treat* OR interven* OR manage* OR admission* OR readmission* OR re-admission* OR hospitaliz* OR hospitalis* OR therap* OR relaps* OR remission* OR recurrent*)) N3 (TI (outcome* OR out-come* OR result* OR endpoint* OR end-point* OR effect* OR	143,930	EditS16

	efficac* OR expect*) OR AB (outcome* OR out-come* OR result* OR endpoint* OR end-point* OR effect* OR efficac* OR expect*))		
S17	(TI (life* OR Lives) OR AB (Life* OR lives*)) N3 (TI expect* OR AB expect*)	4,107	EditS17
S18	(MH "Survival Analysis+") OR (MH "Survival")	69,740	EditS18
S19	(TI kaplan* OR AB kaplan*) N3 (TI meier* OR AB meier*)	3,158	EditS19
S20	(TI product* OR AB product*) N3 (TI (limit* OR model* OR method*) OR AB (limit* OR model* OR method*))	1,897	EditS20
S21	(TI (hazard* OR cox*) OR AB (hazard* OR cox*)) N3 (TI (proportion* OR model* OR regression* OR estimat* OR analys* OR method*) OR AB (proportion* OR model* OR regression* OR estimat* OR analys* OR method*))	10,496	EditS21
S22	S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21	909,232	EditS22
S23	S7 AND S12 AND S22	2,216	EditS23

Search strategy for EMBASE

Database: Embase <1980 to 2014 Week 34>

Search Strategy:

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1 exp heart infarction/ (263885)

2 ((heart* or cardi* or myocardi* or coronar*) adj3 (attack* or infarct* or shock* or stun* or hibernat* or postinfarct* or post-infarct* or reinfarct* or re-infarct* or reperfus* or re-perfus* or ischemi* or ischaemi* or necros* or thromb* or occlus* or atherosclero* or block* or obstruct* or clos* or plug* or clog* or plaqu* or emboli* or clot*)).ti,ab,sh. (546483)

3 (Coronar* adj3 (syndrom* or diseas* or disorder*)).ti,ab,sh. (192970)

4 exp coronary artery thrombosis/ (5911)

5 or/1-4 (692835)

6 exp heart bundle branch block/ (16208)

7 exp heart left bundle branch block/ (5392)

8 exp heart right bundle branch block/ (7735)

9 ((fascic* or bundle* or branch*) adj3 block*).ti,ab,sh. (10303)

10 exp His bundle/ (2630)

11 exp Purkinje fiber/ (2653)

12 ((Purkinje* or kent* or hiss or his) adj3 (fiber* or bundle* or block*)).ti,ab,sh. (5903)

13 or/6-12 (27004)

14 exp prognosis/ (455888)

15 (prognos* or surviv* or futilit* or mortalit* or risk* or hazard* or forecast* or fore-cast* or foretell* or fore-tell* or determin* or predict* or comorbid* or co-morbid* or complicat*).ti,ab,sh. (7241661)

16 (independ* adj3 (indicat* or factor* or influen* or featur* or caus* or element* or reason* or contribut*)).ti,ab,sh. (100948)

17 ((treat* or interven* or manage* or admission* or readmission* or re-admission* or hospitaliz* or hospitalis* or therap* or relaps* or remission* or recurrent*) adj3 (outcome* or out-come* or result* or endpoint* or end-point* or effect* or efficac* or expect*)).ti,ab,sh. (1080412)

18 (Life adj3 expect*).ti,ab,sh. (27351)

19 exp survival/ (618157)

20 exp proportional hazards model/ (43979)

21 ((kaplan* adj2 meier*) or productlimit* or (product* adj3 (limit* or model* or method*)) or ((hazard* or cox*) adj3 (proportion* or model* or regression* or estimat* or analys* or method*))).ti,ab,sh. (168491)

22 or/14-21 (7829364)

23 5 and 13 and 22 (3972)

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Search strategy for Medline

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 exp Myocardial Infarction/ (148189)

2 ((heart* or cardi* or myocardi* or coronar*) adj3 (attack* or infarct* or shock* or stun* or hibernat* or postinfarct* or post-infarct* or reinfarct* or re-infarct* or reperfus* or re-perfus* or ischemi* or ischaemi* or necros* or thromb* or occlus* or atherosclero* or block* or obstruct* or clos* or plug* or clog* or plaqu* or emboli* or clot*)).ti,ab,sh. (326658)

3 (Coronar* adj3 (syndrom* or diseas* or disorder*)).ti,ab,sh. (136438)

4 exp Coronary Thrombosis/ (6101)

5 or/1-4 (440075)

6 exp Bundle-Branch Block/ (7542)

7 ((fascic* or bundle* or branch*) adj3 block*).ti,ab,sh. (8467)

8 exp "Bundle of His"/ (3263)

9 exp Purkinje Fibers/ (2784)

10 ((Purkinje* or kent* or hiss or his) adj3 (fiber* or bundle* or block*)).ti,ab,sh. (6364)

11 or/6-10 (19626)

12 exp Prognosis/ (1117591)

13 (prognos* or surviv* or futilit* or mortalit* or risk* or hazard* or forecast* or fore-cast* or foretell* or fore-tell* or determin* or predict* or comorbid* or co-morbid* or complicat*).ti,ab,sh. (6052026)

14 (independ* adj3 (indicat* or factor* or influen* or featur* or caus* or element* or reason* or contribut*)).ti,ab,sh. (78841)

15 ((treat* or interven* or manage* or admission* or readmission* or re-admission* or hospitaliz* or hospitalis* or therap* or relaps* or remission* or recurrent*) adj3 (outcome* or out-come* or result* or endpoint* or end-point* or effect* or efficac* or expect*)).ti,ab,sh. (744231)

16 (Life adj3 expect*).ti,ab,sh. (21918)

17 exp survival analysis/ (190275)

18 ((kaplan* adj2 meier*) or productlimit* or (product* adj3 (limit* or model* or method*)) or ((hazard* or cox*) adj3 (proportion* or model* or regression* or estimat* or analys* or method*))).ti,ab,sh. (110087)

19 or/12-18 (6741388)

20 5 and 11 and 19 (2243)

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Search strategy for PubMed

Search	Query	Items found
#1	Search **Myocardial Infarction**	198,494
#2	Search **heart attack* [tw] OR heart infarct* [tw] OR heart shock* [tw] OR heart stun* [tw] OR heart hibernat* [tw] OR heart postinfarct* [tw] OR heart post-infarct* [tw] OR heart reinfarct* [tw] OR heart re-infarct* [tw] OR heart reperfus* [tw] OR heart re-perfus* [tw] OR heart ischemi* [tw] OR heart ischaemi* [tw] OR heart necros* [tw] OR heart thrombos* [tw] OR heart occlus* [tw] OR heart atherosclero* [tw] OR heart block* [tw] OR heart obstruct* [tw] OR heart clos* [tw] OR heart plug* [tw] OR heart clog* [tw] OR heart plaqu* [tw] OR heart emboli* [tw] OR heart clot* [tw]**	63,722
#3	Search **Cardiac attack*[tw] OR Cardiac infarct* [tw] OR Cardiac shock* [tw] OR Cardiac stun* [tw] OR Cardiac hibernat* [tw] OR Cardiac postinfarct* [tw] OR Cardiac post-infarct* [tw] OR Cardiac reinfarct* [tw] OR Cardiac re-infarct* [tw] OR Cardiac reperfus* [tw] OR Cardiac re-perfus* [tw] OR Cardiac ischemi* [tw] OR Cardiac ischaemi* [tw] OR Cardiac necros* [tw] OR Cardiac thrombos* [tw] OR Cardiac occlus* [tw] OR Cardiac atherosclero* [tw] OR Cardiac block* [tw] OR Cardiac obstruct* [tw] OR Cardiac clos* [tw] OR Cardiac plug* [tw] OR Cardiac clog* [tw] OR Cardiac plaqu* [tw] OR Cardiac emboli* [tw] OR Cardiac clot* [tw]**	72,671
#4	Search **cardiogenic attack*[tw] OR cardiogenic infarct* [tw] OR cardiogenic shock* [tw] OR cardiogenic stun* [tw] OR cardiogenic hibernat* [tw] OR cardiogenic postinfarct* [tw] OR cardiogenic post-infarct* [tw] OR cardiogenic reinfarct* [tw] OR cardiogenic re-infarct* [tw] OR cardiogenic reperfus* [tw] OR cardiogenic re-perfus* [tw] OR cardiogenic ischemi* [tw] OR cardiogenic ischaemi* [tw] OR cardiogenic necros* [tw] OR cardiogenic thrombos* [tw] OR cardiogenic occlus* [tw] OR cardiogenic atherosclero* [tw] OR cardiogenic block* [tw] OR cardiogenic obstruct* [tw] OR cardiogenic clos* [tw] OR cardiogenic plug* [tw] OR cardiogenic clog* [tw] OR cardiogenic plaqu* [tw] OR cardiogenic emboli* [tw] OR cardiogenic clot* [tw]**	11,413
#5	Search **myocardial attack*[tw] OR myocardial infarct* [tw] OR myocardial shock* [tw] OR myocardial stun* [tw] OR myocardial hibernat* [tw] OR myocardial postinfarct* [tw] OR myocardial post-infarct* [tw] OR myocardial reinfarct* [tw] OR myocardial re-infarct* [tw] OR myocardial reperfus* [tw] OR myocardial re-perfus* [tw] OR myocardial ischemi* [tw] OR myocardial ischaemi* [tw] OR myocardial necros* [tw] OR myocardial thrombos* [tw] OR myocardial occlus* [tw] OR myocardial atherosclero* [tw] OR myocardial block* [tw] OR myocardial obstruct* [tw] OR myocardial clos* [tw] OR myocardial plug* [tw] OR myocardial clog* [tw] OR myocardial plaqu* [tw] OR myocardial emboli* [tw] OR myocardial clot* [tw]**	278,886
#6	Search **Coronary infarct* [tw] OR Coronary hibernat* [tw] OR Coronary postinfarct* [tw] OR Coronary post-infarct* [tw] OR Coronary reinfarct* [tw] OR Coronary re-infarct* [tw] OR Coronary reperfus* [tw] OR Coronary re-perfus* [tw] OR Coronary ischemi* [tw] OR Coronary ischaemi* [tw] OR Coronary necros* [tw] OR Coronary thrombos* [tw] OR Coronary occlus* [tw] OR Coronary atherosclero* [tw] OR Coronary block* [tw] OR Coronary obstruct* [tw] OR Coronary clos* [tw] OR Coronary plug* [tw] OR Coronary clog* [tw] OR Coronary plaqu* [tw] OR Coronary emboli* [tw] OR Coronary clot* [tw]**	54,341
#7	Search **coronaries infarct* [tw] OR coronaries hibernat* [tw] OR coronaries**	686

	postinfarct* [tw] OR coronaries post-infarct* [tw] OR coronaries reinfarct* [tw] OR coronaries re-infarct* [tw] OR coronaries reperfus* [tw] OR coronaries re-perfus* [tw] OR coronaries ischemi* [tw] OR coronaries ischaemi* [tw] OR coronaries necros* [tw] OR coronaries thrombos* [tw] OR coronaries occlus* [tw] OR coronaries atherosclero* [tw] OR coronaries block* [tw] OR coronaries obstruct* [tw] OR coronaries clos* [tw] OR coronaries plug* [tw] OR coronaries clog* [tw] OR coronaries plaqu* [tw] OR coronaries emboli* [tw] OR coronaries clot* [tw]	
#8	Search **Coronary syndrom* [tw] OR Coronary diseas* [tw] OR Coronary disorder* [tw]**	149,518
#9	Search **Coronaries syndrom* [tw] OR Coronaries diseas* [tw] OR Coronaries disorder* [tw]**	709
#10	Search **Coronary Thrombosis**	20,150
#11	Search **#1 OR #2 OR #3 OR #4 OR #5 OR #7 OR #8 OR #9 OR #10**	469,558
#12	Search **Bundle-Branch Block**	11,100
#13	Search **Fascicular block* [tw] OR Fasciculi block* [tw] OR Bundle block* [tw] OR Bundles block* [tw] OR Branch block* [tw] OR Branches block* [tw]**	13,986
#14	Search **Bundle of His**	5,450
#15	Search **Purkinje Fibers**	5,241
#16	Search **Purkinje Fiber* [tw] OR Kent Fiber* [tw] OR hiss Fiber* [tw] OR his Fiber* [tw]**	4,858
#17	Search **Purkinje Bundle* [tw] OR Kent Bundle* [tw] OR hiss Bundle*[tw] OR his Bundle* [tw]**	2,653
#18	Search **Purkinje block* [tw] OR Kent block* [tw] OR hiss block* [tw] OR his block* [tw]**	797
#19	Search **#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18**	24,990
#20	Search **Prognosis**	1,212,451
#21	Search **prognos* [tw] OR surviv* [tw] OR futilit* [tw] OR mortalit* [tw] OR risk* [tw] OR hazard* [tw] OR forecast* [tw] OR fore-cast* [tw] OR foretell* [tw] OR fore-tell* [tw] OR determin* [tw] OR predict* [tw] OR comorbid* [tw] OR co-morbid* [tw] OR complicat* [tw]**	7,458,485
#22	Search **Independent indicat* [tw] OR Independent factor* [tw] OR Independent influen* [tw] OR Independent featur* [tw] OR Independent caus* [tw] OR Independent element* [tw] OR Independent reason* [tw] OR Independent contribut* [tw]**	12,730
#23	Search **Treatment outcome* [tw] OR treatments outcome* [tw] OR Intervention outcome* [tw] OR interventions outcome* [tw] OR Management outcome* [tw] OR managements outcome* [tw] OR Admission outcome* [tw] OR admissions outcome* [tw] OR Readmission outcome* [tw] OR Readmissions outcome* [tw] OR re-admission outcome* [tw] OR re-admissions outcome* [tw] OR hospitalization outcome* [tw] OR hospitalizations outcome* [tw] OR therapy outcome* [tw] OR therapies outcome* [tw] OR relapse outcome* [tw] OR remission outcome* [tw] OR recurrent outcome* [tw]**	885,841
#24	Search **Treatment out-come* [tw] OR treatments out-come* [tw] OR Intervention out-come* [tw] OR interventions out-come* [tw] OR Management out-come* [tw] OR managements out-come* [tw] OR Admission out-come* [tw] OR admissions out-**	294

	come* [tw] OR Readmission out-come* [tw] OR Readmissions out-come* [tw] OR re-admission out-come* [tw] OR re-admissions out-come* [tw] OR hospitalization out-come* [tw] OR hospitalizations out-come* [tw] OR therapy out-come* [tw] OR therapies out-come* [tw] OR relapse out-come* [tw] OR remission out-come* [tw] OR recurrent out-come* [tw]	
#25	Search **Treatment result* [tw] OR treatments result* [tw] OR Intervention result* [tw] OR interventions result* [tw] OR Management result* [tw] OR managements result* [tw] OR Admission result* [tw] OR admissions result* [tw] OR Readmission result* [tw] OR Readmissions result* [tw] OR re-admission result* [tw] OR re-admissions result* [tw] OR hospitalization result* [tw] OR hospitalizations result* [tw] OR therapy result* [tw] OR therapies result* [tw] OR relapse result* [tw] OR remission result* [tw] OR recurrent result* [tw]**	38,781
#26	Search **Treatment endpoint* [tw] OR treatments endpoint* [tw] OR Intervention endpoint* [tw] OR interventions endpoint* [tw] OR Management endpoint* [tw] OR managements endpoint* [tw] OR Admission endpoint* [tw] OR admissions endpoint* [tw] OR Readmission endpoint* [tw] OR Readmissions endpoint* [tw] OR re-admission endpoint* [tw] OR re-admissions endpoint* [tw] OR hospitalization endpoint* [tw] OR hospitalizations endpoint* [tw] OR therapy endpoint* [tw] OR therapies endpoint* [tw] OR relapse endpoint* [tw] OR remission endpoint* [tw] OR recurrent endpoint* [tw]**	31,363
#27	Search **Treatment end-point* [tw] OR treatments end-point* [tw] OR Intervention end-point* [tw] OR interventions end-point* [tw] OR Management end-point* [tw] OR managements end-point* [tw] OR Admission end-point* [tw] OR admissions end-point* [tw] OR Readmission end-point* [tw] OR Readmissions end-point* [tw] OR re-admission end-point* [tw] OR re-admissions end-point* [tw] OR hospitalization end-point* [tw] OR hospitalizations end-point* [tw] OR therapies end-point* [tw] OR relapse end-point* [tw] OR remission end-point* [tw] OR recurrent end-point* [tw]**	24,695
#28	Search **Treatment effect* [tw] OR treatments effect* [tw] OR Intervention effect* [tw] OR interventions effect* [tw] OR Management effect* [tw] OR managements effect* [tw] OR Admission effect* [tw] OR admissions effect* [tw] OR Readmission effect* [tw] OR Readmissions effect* [tw] OR re-admission effect* [tw] OR re-admissions effect* [tw] OR hospitalization effect* [tw] OR hospitalizations effect* [tw] OR therapy effect* [tw] OR therapies effect* [tw] OR relapse effect* [tw] OR remission effect* [tw] OR recurrent effect* [tw]**	124,569
#29	Search **Treatment efficac* [tw] OR treatments efficac* [tw] OR Intervention efficac* [tw] OR interventions efficac* [tw] OR Management efficac* [tw] OR managements efficac* [tw] OR Admission efficac* [tw] OR admissions efficac* [tw] OR Readmission efficac* [tw] OR Readmissions efficac* [tw] OR re-admission efficac* [tw] OR re-admissions efficac* [tw] OR hospitalization efficac* [tw] OR hospitalizations efficac* [tw] OR therapy efficac* [tw] OR therapies efficac* [tw]**	22,764
#30	Search **Treatment expect* [tw] OR treatments expect* [tw] OR Intervention expect* [tw] OR interventions expect* [tw] OR Management expect* [tw] OR managements expect* [tw] OR Admission expect* [tw] OR admissions expect* [tw] OR Readmission expect* [tw] OR Readmissions expect* [tw] OR re-admission expect* [tw] OR re-admissions expect* [tw] OR hospitalization expect* [tw] OR hospitalizations expect* [tw] OR therapy expect* [tw] OR therapies expect* [tw] OR relapse expect* [tw] OR remission expect* [tw] OR recurrent expect* [tw]**	830,16
#31	Search **hospitalisation expect* [tw] OR hospitalisation efficac* [tw] OR**	147,587

	hospitalisation effect* [tw] OR hospitalisation end-point* [tw] OR hospitalisations endpoint* [tw] OR hospitalisation result* [tw] OR hospitalisation out-come* [tw] OR hospitalisation outcome* [tw]	
#32	Search **Life expect* [tw] OR Lives expect* [tw]**	31,148
#33	Search **kaplan meier* [tw] OR product limit* [tw] OR product model* [tw] OR product method* [tw] OR hazard proportion* [tw] OR hazard model* [tw] OR hazard estimat* [tw] OR hazard analys* [tw] OR hazard method* [tw] OR cox proportion* [tw] OR cox model* [tw] OR cox regression* [tw] OR cox estimat* [tw] OR cox analys* [tw] OR cox method* [tw]**	98,652
#34	Search **#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33**	7,873,397
#35	Search **#11 AND #19 AND #34**	4,696

Appendix 2. Data Abstraction form.

Table 1: characteristics of included studies							
Study Name	**Study design/ funding**	**Sample size**	**Participants**	**Exposure**	**Comparison**	**Outcomes**	**Country**

Table 2: risk of bias in included studies					
Study name	**Developing and applying appropriate eligibility criteria**	**Exposure measurement**	**Outcome measurement**	**Controlling for confounding**	**Completeness of data**

Table 3A: statistical data (Adjusted one year mortality).					
Study Name	**Outcome**	**Summary statistic**	**Point effect estimate**	**95% Confidence Interval**	**P value**

Table 3B. Studies reported raw data. (One year mortality).					
Study name	Measurement F/U time	Exposed group		Comparison group	
		No. of exposed	Death rate	No. comparison	Death rate

Table 4A: statistical data (Adjusted In- hospital mortality).					
Study Name	**Outcome**	**Summary statistic**	**Point effect estimate**	**95% Confidence Interval**	**P value**

Table 4B: statistical data (Un adjusted In- hospital mortality).					
Study Name	**Outcome**	**Summary statistic**	**Point effect estimate**	**95% Confidence Interval**	**P value**

Table 4C. Studies reported raw data. (In-hospital mortality).					
Study name	Measurement F/U time	Exposed group		Comparison group	
		No. of exposed	Death rate	No. comparison	Death rate

Table 5. Studies reported raw data.					
Study name	Measurement F/U time	Exposed group		Comparison group	
		No. of exposed	Event rate	No. comparison	Event rate

References

Al-Faleh, H., Fu, Y., Wagner, G., Goodman, S., Sgarbossa, E., Granger, C., . . . ASSENT 2 and 3 Investigators. (2006). Unraveling the spectrum of left bundle branch block in acute myocardial infarction: Insights from the assessment of the safety and efficacy of a new thrombolytic (ASSENT 2 and 3) trials. *American Heart Journal, 151*(1), 10-15. doi:S0002-8703(05)00259-0 [pii]

Azadani, P. N., Soleimanirahbar, A., Marcus, G. M., Haight, T. J., Hollenberg, M., Olgin, J. E., & Lee, B. K. (2012). Asymptomatic left bundle branch block predicts new-onset congestive heart failure and death from cardiovascular diseases. *Cardiology Research, 3*(6), 258-263. doi:http://dx.doi.org/10.4021/cr214w

Bhalli, M. A., Khan, M. Q., Samore, N. A., & Mehreen, S. (2009). Frequency and clinical outcome in conduction defects in acute myocardial infarction. *Journal of Ayub Medical College, Abbottabad : JAMC, 21*(3), 32-37.

Brembilla-Perrot, B., Alla, F., Suty-Selton, C., Huttin, O., Blangy, H., Sadoul, N., . . . Juilliere, Y. (2008). Nonischemic dilated cardiomyopathy: Results of noninvasive and invasive evaluation in 310 patients and clinical significance of bundle branch block. *Pacing & Clinical Electrophysiology, 31*(11), 1383-1390.

Brilakis, E. S., Wright, R. S., Kopecky, S. L., Reeder, G. S., Williams, B. A., & Miller, W. L. (2001). Bundle branch block as a predictor of long-term survival after acute myocardial infarction. *The American Journal of Cardiology, 88*(3), 205-209. doi:http://dx.doi.org/10.1016/S0002-9149(01)01626-5

Brown, A. J., Hoole, S. P., McCormick, L. M., Malone-Lee, M., Cacciottolo, P. J., Schofield, P. M., & West, N. E. (2013). Left bundle branch block with acute thrombotic occlusion is associated with increased myocardial jeopardy score and poor clinical outcomes in primary percutaneous coronary intervention activations. *Heart, 99*(11), 774-778. doi:http://dx.doi.org/10.1136/heartjnl-2012-303194

Bussink, B. E., Holst, A. G., Jespersen, L., Deckers, J. W., Jensen, G. B., & Prescott, E. (2013). Right bundle branch block: Prevalence, risk factors, and outcome in the general population: Results from the copenhagen city heart study. *European Heart Journal, 34*(2), 138-146. doi:10.1093/eurheartj/ehs291 [doi]

Chang, A. M., Shofer, F. S., Tabas, J. A., Magid, D. J., McCusker, C. M., & Hollander, J. E. (2009). Lack of association between left bundle-branch block and acute myocardial infarction in symptomatic ED patients. *American Journal of Emergency Medicine, 27*(8), 916-921.

Cleempoel, H., Vainsel, H., Bernard, R., Dramaix, M., Lenaers, A., Van Kuyk, M., . . . Vandenbossche, J. L. (1986). Predictors of early death after acute myocardial infarction: Two months follow-up. *European Heart Journal, 7*(4), 305-311.

Emergency department: Rapid identification and treatment of patients with acute myocardial Infarction—National heart attack alert program coordinating committee. (1994). *Annals of Emergency Medicine, 23*(2), 311-329. doi:http://dx.doi.org/10.1016/S0196-0644(94)70045-1

Go, A. S., Barron, H. V., Rundle, A. C., Ornato, J. P., & Avins, A. L. (1998). Bundle-branch block and in-hospital mortality in acute myocardial infarction. national

registry of myocardial infarction 2 investigators. *Annals of Internal Medicine, 129*(9), 690-697.

Guerrero, M., Harjai, K., Stone, G. W., Brodie, B., Cox, D., Boura, J., . . . Grines, C. (2005). Comparison of the prognostic effect of left versus right versus no bundle branch block on presenting electrocardiogram in acute myocardial infarction patients treated with primary angioplasty in the primary angioplasty in myocardial infarction trials. *American Journal of Cardiology, 96*(4), 482-488.

Gunnarsson, G., Eriksson, P., & Dellborg, M. (2000). Bundle branch block and acute myocardial infarction. treatment and outcome. *Scandinavian Cardiovascular Journal, 34*(6), 575-579.

Hazem, A., Sharma, S., Sharma, A., Leitch, C., Sharadanant, R., Uriell, M., . . . Murad, M. H. (2014). Abstract 309: Is right bundle branch block associated with poor outcomes in the setting of an acute coronary syndrome? A systematic review and meta-analysis. *Circulation: Cardiovascular Quality and Outcomes, 7*(Suppl 1), A309-A309.

Higgins, J. P. T., Thompson, S. G., Deeks, J. J., Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *British Medical Journal, 327,* 557-560.

Imanishi, R., Seto, S., Ichimaru, S., Nakashima, E., Yano, K., & Akahoshi, M. (2006). Prognostic significance of incident complete left bundle branch block observed over a 40-year period. *American Journal of Cardiology, 98*(5), 644-648.

Jain, A. C., & Mehta, M. C. (2003). Etiologies of left bundle branch block and correlations with hemodynamic and angiographic findings. *The American*

Journal of Cardiology, 91(11), 1375-1378. doi:http://dx.doi.org/10.1016/S0002-9149(03)00337-0

Jain, S., Ting, H. T., Bell, M., Bjerke, C. M., Lennon, R. J., Gersh, B. J., . . . Prasad, A. (2011). Utility of left bundle branch block as a diagnostic criterion for acute myocardial infarction. *The American Journal of Cardiology, 107*(8), 1111-1116. doi:http://dx.doi.org/10.1016/j.amjcard.2010.12.007

Jim, M. H., Chan, A. O., Tse, H. F., & Lau, C. P. (2009). Predictors of inhospital outcome after acute inferior wall myocardial infarction. *Singapore Medical Journal, 50*(10), 956-961.

Kleemann, T., Juenger, C., Gitt, A. K., Schiele, R., Schneider, S., Senges, J., . . . MITRA PLUS Study Group. (2008). Incidence and clinical impact of right bundle branch block in patients with acute myocardial infarction: ST elevation myocardial infarction versus non-ST elevation myocardial infarction. *American Heart Journal, 156*(2), 256-261. doi:10.1016/j.ahj.2008.03.003 [doi]

Kontos, M. C., Aziz, H. A., Chau, V. Q., Roberts, C. S., Ornato, J. P., & Vetrovec, G. W. (2011). Outcomes in patients with chronicity of left bundle-branch block with possible acute myocardial infarction. *American Heart Journal, 161*(4), 698-704. doi:http://dx.doi.org/10.1016/j.ahj.2011.01.008

Miller, W. L., Sgura, F. A., Kopecky, S. L., Asirvatham, S. J., Williams, B. A., Wright, R. S., & Reeder, G. S. (2001). Characteristics of presenting electrocardiograms of acute myocardial infarction from a community-based population predict short- and long-term mortality. *American Journal of Cardiology, 87*(9), 1045-1050.

Moser, Debra K.,Riegel, Barbara,,. (2008). *Cardiac nursing : A companion to braunwald's heart disease*. St. Louis, Missouri ; Edinburgh: Saunders/Elsevier.

Nazif, T. M., Williams, M. R., Hahn, R. T., Kapadia, S., Babaliaros, V., Rodes-Cabau, J., . . . Kodali, S. K. (2014). Clinical implications of new-onset left bundle branch block after transcatheter aortic valve replacement: Analysis of the PARTNER experience. *European Heart Journal, 35*(24), 1599-1607. doi:10.1093/eurheartj/eht376 [doi]

Neeland, I. J., Kontos, M. C., & de Lemos, J. A. (2012). Evolving considerations in the management of patients with left bundle branch block and suspected myocardial infarction. *Journal of the American College of Cardiology, 60*(2), 96-105. doi:10.1016/j.jacc.2012.02.054 [doi]

O'Gara, P. T., Kushner, F. G., Ascheim, D. D., Casey, D. E., Chung, M. K., de Lemos, J. A., . . . Zhao, D. X. (2013). 2013 ACCF/AHA guideline for the management of ST-elevation myocardial InfarctionA report of the american college of cardiology foundation/american heart association task force on practice guidelines. *Journal of the American College of Cardiology, 61*(4), e78-e140. doi:10.1016/j.jacc.2012.11.019

Sgarbossa, E. B., Pinski, S. L., Barbagelata, A., Underwood, D. A., Gates, K. B., Topol, E. J., . . . Wagner, G. S. (1996). Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. GUSTO-1 (global utilization of streptokinase and tissue plasminogen activator for occluded coronary arteries) investigators. *The New England Journal of Medicine, 334*(8), 481-487. doi:10.1056/NEJM199602223340801 [doi]

Sgarbossa, E. B., Pinski, S. L., Topol, E. J., Califf, R. M., Barbagelata, A., Goodman, S. G., . . . Wagner, G. S. (1998). Acute myocardial infarction and complete bundle branch block at hospital admission: Clinical characteristics and outcome in the thrombolytic era. GUSTO-I investigators global utilization of streptokinase and t-PA [tissue-type plasminogen activator] for occluded coronary arteries. *Journal of the American College of Cardiology, 31*(1), 105-110.

Sorensen, J. T., Stengaard, C., Sorensen, C. A., Thygesen, K., Botker, H. E., Thuesen, L., & Terkelsen, C. J. (2013). Diagnosis and outcome in a prehospital cohort of patients with bundle branch block and suspected acute myocardial infarction. *European Heart Journal Acute Cardiovascular Care, 2*(2), 176-181. doi:http://dx.doi.org/10.1177/2048872613483591

Steg, P. G., James, S. K., Atar, D., Badano, L. P., Lundqvist, C. B., . . . Wallentin, L. (2012). ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal, 33(20), 2569-2619.

Stenestrand, U., Tabrizi, F., Lindback, J., Englund, A., Rosenqvist, M., & Wallentin, L. (2004). Comorbidity and myocardial dysfunction are the main explanations for the higher 1-year mortality in acute myocardial infarction with left bundle-branch block. *Circulation, 110*(14), 1896-1902. doi:10.1161/01.CIR.0000143136.51424.38 [doi]

Terkelsen, C. J., Lassen, J. F., Norgaard, B. L., Gerdes, J. C., Jensen, T., Gotzsche, L. B., . . . Andersen, H. R. (2005). Mortality rates in patients with ST-elevation vs.

non-ST-elevation acute myocardial infarction: Observations from an unselected cohort. *European Heart Journal, 26*(1), 18-26.

Ting, P., Chua, T. S., Wong, A., Sim, L. L., Tan, V. W., & Koh, T. H. (2007). Trends in mortality from acute myocardial infarction in the coronary care unit. *Annals of the Academy of Medicine, Singapore, 36*(12), 974-979.

Van de Werf, F. (1999). Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: The ASSENT-2 double-blind randomised trial. *The Lancet, 354*(9180), 716-722. doi:http://dx.doi.org/10.1016/S0140-6736(99)07403-6

Wallentin, L., Goldstein, P., Armstrong, P. W., Granger, C. B., Adgey, A. A. J., Arntz, H. R., . . . Van de Werf, F. (2003). Efficacy and safety of tenecteplase in combination with the low-molecular-weight heparin enoxaparin or unfractionated heparin in the prehospital setting: The assessment of the safety and efficacy of a new thrombolytic regimen (ASSENT)-3 PLUS randomized trial in acute myocardial infarction. *Circulation, 108*(2), 135-142. doi:10.1161/01.CIR.0000081659.72985.A8

White, H., & =Hirulog and Early Reperfusion or Occlusion (HERO)-2,Trial Investigators. (2001). Thrombin-specific anticoagulation with bivalirudin versus heparin in patients receiving fibrinolytic therapy for acute myocardial infarction: The HERO-2 randomised trial. *Lancet, 358*(9296), 1855-1863. doi:10.1016/s0140-6736(01)06887-8

Widimsky, P., Rohac, F., Stasek, J., Kala, P., Rokyta, R., Kuzmanov, B., . . . Lorencova, A. (2012). Primary angioplasty in acute myocardial infarction with

right bundle branch block: Should new onset right bundle branch block be added to future guidelines as an indication for reperfusion therapy?. *European Heart Journal, 33*(1), 86-95. doi:http://dx.doi.org/10.1093/eurheartj/ehr291

Wong, C. K., Stewart, R. A., Gao, W., French, J. K., Raffel, C., & White, H. D. (2006). Prognostic differences between different types of bundle branch block during the early phase of acute myocardial infarction: Insights from the hirulog and early reperfusion or occlusion (HERO)-2 trial. *European Heart Journal, 27*(1), 21-28.

Yeo, K. K., Li, S., Amsterdam, E. A., Wang, T. Y., Bhatt, D. L., Saucedo, J. F., . . . French, W. J. (2012a). Comparison of clinical characteristics, treatments and outcomes of patients with ST-elevation acute myocardial infarction with versus without new or presumed new left bundle branch block (from NCDR). *American Journal of Cardiology, 109*(4), 497-501. doi:http://dx.doi.org/10.1016/j.amjcard.2011.09.040