ABSTRACT

Background: There are important knowledge gaps in type 2 myocardial infarction (T2MI). Our primary objective was to compare the outcomes of patients with T2MI with those of patients with type 1 myocardial infarction (T1MI). Our secondary objective was to determine whether randomized controlled trials (RCTs) evaluating dual antiplatelet therapy (DAPT) have explicitly included patients with T2MI.

Methods: We performed a meta-analysis comparing outcomes of patients with T2MI with patients with T1MI and a separate systematic review to evaluate the inclusion of T2MI in RCTs evaluating DAPT. There were 19 cohorts enrolling 48,829 patients (40,604 with T1MI and 5361 with T2MI) and 51 RCTs enrolling 188,132 patients with acute coronary syndrome.

The term "type 2 myocardial infarction" (T2MI) was first defined by the Second Universal Definition of Myocardial Infarction 20071 and was recently updated in 2018 by the Task Force for the Fourth Universal Definition of Myocardial Infarction.2 T2MI was defined as myocardial infarction (MI) whereby a condition other than atherosclerotic coronary artery disease creates an imbalance between myocardial oxygen supply and demand.1 Currently, there are no formal management guidelines for patients with T2MI.

Dual antiplatelet therapy (DAPT) (aspirin plus a direct or indirect P2Y12 inhibitor) is the cornerstone in the management of patients with myocardial infarctions secondary to atherosclerotic coronary plaque rupture (T1MI).3,4 However, it remains unclear to what extent DAPT has been evaluated in T2MI. Because platelet activation may be less prominent in T2MI, DAPT may not confer the same benefits as in T1MI.
Results: Patients with T2MI had approximately 2-fold increases in unadjusted odds of long-term mortality compared with patients with T1MI (odds ratio, 2.47; 95% confidence interval, 2.06-2.96; \( P < 0.0001 \)) and a 45% increase in adjusted odds of long-term mortality (odds ratio, 1.45; 95% confidence interval, 1.25-1.69; \( P < 0.0001 \), respectively). There was no published evaluation of efficacy, effectiveness, and safety of DAPT in patients with T2MI.

Conclusion: Patients with T2MI are at increased risk of adjusted all-cause long-term mortality compared with patients with T1MI. The role of DAPT remains unclear in T2MI.

Methods
We performed a systematic review and meta-analysis following the standards set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and the guidelines for reporting meta-analysis of observational studies as proposed by the MOOSE group. We conducted 2 independent literature searches in PubMed, EMBASE, and Science Direct. The first search aimed to identify any studies pertaining directly to T2MI. We used the following search terms: type 2 myocardial infarction, secondary MI, supply-demand mismatch, demand ischemia, secondary ischemia, myocardial ischemia, type 2 ischemia, myocardial injury, myocardial necrosis, and silent ischemia. The second search targeted all studies evaluating DAPT in acute coronary syndrome (ACS) using the keywords myocardial infarction, acute coronary syndrome, clopidogrel, prasugrel, ticagrelor, and heart attack. We specifically excluded RCTs evaluating ticlodipine because this drug is rarely if ever used in this contemporary era. Both searches had no language restriction and covered all studies published since 1999 (release of the first DAPT trial Clopidogrel in Unstable Angina to Prevent Recurrent Ischemic Events [CURE]) to February 12, 2020.

We used the definitions of T1MI and T2MI as defined by the Fourth Universal Definition of Myocardial Infarction. We defined reinfarction as reported in each publication. We additionally included any available RCTs or observational studies of T2MI. We excluded editorials, reviews, letters, animal studies, case reports, and conference abstracts. We also excluded studies that evaluated exclusively postoperative myocardial infarction because the term “T2MI” vs postoperative troponin elevation and myocardial injury was often interchangeably used in these instances. Furthermore, the management and outcomes of these patients were inconsistently described. We excluded observational studies that did not report the rates or number of events for T2MI and T1MI separately. For the second search, we included all RCTs that evaluated DAPT in ACS to determine whether any of these trials specifically included patients with T2MI.

Three reviewers (CR, AAT, and TH) extracted data independently. Disagreements were resolved by consensus and the third reviewer (TH). We extracted data about baseline characteristics of study subjects (age, sex, and comorbidities), management, study inclusion and exclusion criteria, and in-hospital and long-term mortality and reinfarction.

We summarized the outcomes (short/intermediate and long-term all-cause mortality and reinfarction). We defined short/intermediate-term mortality as all deaths occurring at less than 1 year and long-term mortality as all deaths occurring during a follow-up of at least 1 year. We computed weighted means of baseline characteristics and rates of outcomes. We pooled the unadjusted and adjusted comparisons of long-term mortality of patients with T1MI and T2MI of the observational studies. We examined the funnel plot to identify potential publication bias. All meta-analyses were completed with random-effects models with Comprehensive Meta-Analysis, Version 3, 2014. We chose random-effect models because of the marked heterogeneity seen in the fixed-effect models.

Results
We retrieved 2048 citations of studies of T2MI and 1669 citations of studies evaluating DAPT in ACS (Fig. 1). For the final evaluation, we retained 19 cohorts enrolling 48,829 patients (43,468 with T1MI and 5361 with T2MI)\(^9-27\) (Table 1) and 51 RCTs enrolling 188,132 patients\(^25-77\) (Fig. 1). We described the characteristics of the patients enrolled in the observational studies in Supplemental Table S1. No RCTs evaluating DAPT in ACS have explicitly included patients with T2MI. The effectiveness and safety of DAPT were also not appraised in any observational study of T2MI.

Compared with patients with T1MI, patients with T2MI were older (69 vs 65 years, \( P = 0.02 \)), more often female (44% vs 30%, \( P < 0.0001 \)), and more often had diabetes mellitus (30% vs 27%) and hypertension (70% vs 67%, \( P = 0.03 \))
DAPT use in patients with T2MI was reported in only 7 observational studies.\textsuperscript{7,8,13,15,17,19,21,23} The aggregate mean use was 20.8% in patients with T2MI and 74.2% in patients with T1MI (Table 3). Patients with T2MI were 91% less likely to use DAPT and 80% less likely to undergo percutaneous coronary intervention (Table 3).

Patients enrolled in the RCTs had the best unadjusted long-term survival compared with patients with T1MI and T2MI in the observational studies. Compared with patients with T1MI, patients with T2MI had 2.5-fold increase in unadjusted long-term mortality (Table 3 and Fig. 2) and an approximately 45% increase in adjusted long-term mortality (odds ratio, 1.45; 95% confidence interval, 1.25-1.69; \( P < 0.0001 \) (Table 3 and Fig. 3). The comparisons of long-term mortality between T2MI and T1MI were generally adjusted for age, sex, baseline characteristics, and comorbidities, except for the study by Newman et al.,\textsuperscript{15} in which long-term mortality was adjusted only for age, sex, and prior coronary artery disease.

The precipitating factors of T2MI were reported in 7 studies.\textsuperscript{7-9,12,14,21-22} Arrhythmia, anemia/bleeding, respiratory diseases, heart failure, and infection/sepsis were the most common reported precipitating factors for T2MI (Table 4). There was no obvious publication bias detected as the funnel plot appeared to be symmetrical (Fig. 4).

**Discussion**

Our meta-analysis of observational studies showed that compared with patients with T1MI, patients with T2MI were older and more often female, had more hypertension, and had diabetes mellitus. Compared with patients with T1MI, patients with T2MI were 90% less likely to be treated with DAPT and 80% less likely to undergo percutaneous coronary intervention. Patients with T2MI had approximately 45% increase in adjusted odds of all-cause long-term mortality compared with patients with T1MI. The efficacy, effectiveness, and safety of DAPT have never been formally appraised in RCTs or observational studies.

There were marked differences in unadjusted short- and long-term mortality rates among the 3 groups of patients (patients with ACS enrolled in the RCTs, T1MI, and T2MI in the observational cohorts). Although both short- and long-term mortality were less than 5% in patients with ACS enrolled in the RCTs that evaluated DAPT, unadjusted short- and long-term mortality were 7% and 11%, respectively, for patients with T1MI in the observational studies. The higher unadjusted short- and long-term mortality of patients in the observational studies likely would be due to the enrollment of patients without MI, with younger age, and with fewer comorbid conditions in the RCTs than patients in the observational studies.\textsuperscript{7,8}
| Study first author (year of publication) | Design                        | Countries                  | Enrollment periods | No. of patients with MI | No. of centres/ countries | Key inclusion criteria                                                                 | Key exclusion criteria                                                                 |
|----------------------------------------|-------------------------------|----------------------------|-------------------|-------------------------|--------------------------|----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Arora (2018)                           | Retrospective                 | United States              | 2013-2014         | 1039                    | Single centre            | All patients with NSTEMI                                                                | STEMI transferred in, no available troponins, cardiac arrest                             |
| Baron (2014)                           | Prospective (SWEDEHEART Study) | Sweden                     | 2011              | 18,891                  | 73 Swedish hospitals    | MI hospitalized in Sweden                                                            | None                                                                                   |
| Cediel (2016)                          | Retrospective                 | Spain                      | 2012-2013         | 570                     | Single university centre | All adults with at least 1 value of troponin tested                                   | Cardiac arrest, alternate diagnoses other than MI, lived far                             |
| Chapman (2018)                         | Prospective                   | Scotland                   | 2009-2009         | 1600                    | 1 tertiary centre       | All patients with elevated troponin values                                            | Admitted for elective procedures, incomplete electronic hospital records, and nonresidents |
| Gonzalez (2011)                        | Retrospective                 | United States              | 2004-2007         | 348                     | 1 tertiary centre       | All MI with ≥ 50% coronary stenosis on angiogram and ≥ 24-mo follow-up              | Terminal diseases, refused standard MI treatment, no obstructive coronary artery disease |
| Greenslade (2017)                      | Pooled study of 1 prospective observational and 1 interventional study | Australia              | 2008-2014         | 152                     | Single tertiary centre   | Adults with MI who could provide consent, enrollment during regular working hours   | Pregnant, lived far                                                                      |
| Javed (2009)                           | Prospective                   | United States              | 2009              | 207                     | Single centre           | All adults with ≥ 1 abnormal troponin value who provided consent                     | Refusal to participate                                                                   |
| Lambrecht (2018)                       | Prospective study             | Denmark                    | 2010              | 479                     | Single centre           | All patients with at least 1 troponin ≥ 99th percentile normal value                  | Pregnant, lived outside catchment area                                                  |
| Lopez-Cuenca (2016)                    | Retrospective                 | Spain                      | 2012-2013         | 824                     | Single veterans tertiary centre | All patients with MI                                                               | None                                                                                   |
| Nestelberger (2017)                    | Retrospective                 | Switzerland, Italy, Germany, Spain, Poland | 2006-2015 | 924                     | 12 centres/5 countries | Adults within 12 h of ischemic symptoms                                               | Unclear diagnosis                                                                        |
| Neumann (2017)                         | Prospective                   | Germany                    | 2013-2016         | 287                     | Single university centre | Adults with suspected MI who could provide consent                                   | Missing troponins, STEMI                                                                 |
| Radovanovic (2016)                     | Prospective (AMIS-PLUS)       | Switzerland                | 2009-2015         | 14,920                  | 53 Swiss hospitals      | All patients hospitalized with MI in Switzerland                                       | None                                                                                   |
| Raphael (2020)                         | Prospective                   | United States              | 2003-2012         | 2, 436                  | Mayo Clinic and Olmstead Medical Center | Adults with ≥ 1 available troponin value                                                | Prior MI, refused to consent, unclear cause for elevation of troponin                   |
| Saaby (2014)                           | Prospective                   | Denmark                    | 2010              | 488                     | Single centre           | Adults with ≥ 1 available troponin value                                                | Outside catchment area, troponins administered outside the hospital                     |
| Study first author (year of publication) | Design | Countries | Enrollment periods | No. of patients with MI | No. of centres/countries | Key inclusion criteria | Key exclusion criteria |
|-----------------------------------------|--------|-----------|--------------------|------------------------|--------------------------|-----------------------|-----------------------|
| Sandoval (2015)                         | Retrospective | United States | 2013             | 310                     | Single centre            | Adults with ≥ 1 available troponin value | None |
| Sandoval (2017)                         | Prospective (UTROPIA Study) | United States | 2011             | 217                     | Single centre            | All patients who provided consent and with troponins and 1 ECG within 24 h | Pregnant, transferred in patients, did not present to the emergency department |
| Shah (2015)                             | Prospective | Scotland    | 2014             | 1600                    | Single centre            | All patients with troponin I ≥ 50 ng/L | None |
| Smilowitz (2018)                        | Prospective | United States | 2012-2013        | 283                     | Single veterans tertiary centre | All patients with elevated troponin values | None |
| Stein (2014)                            | Prospective | Israel      | 2008-2010        | 2818                    | Nationwide Israel multicentres (26 intensive and 37 medical wards) | All patients with MI | None |

ACIS, Acute Coronary Syndrome Israeli Survey; AMIS-PLUS, National Registry of Acute Myocardial Infarction in Switzerland; ECG, electrocardiogram; MI, myocardial infarction; NSTEMI, non-ST-segment myocardial infarction; STEMI, ST-segment elevation myocardial infarction; SWEDHEART, Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies; T1MI, type 1 myocardial infarction; T2MI, type 2 myocardial infarction; UTROPIA, Use of Troponin in Acute Coronary Syndromes.

The lack of significant heterogeneity in our random-effects model of adjusted odds was markedly in contrast to the heterogeneity observed in the random-effects model of unadjusted odds.

In a meta-analysis of 9 observational studies, Gupta et al. reported a 3-fold increase in short and intermediate-term mortality in patients with T2MI compared with patients with T1MI. In our study, provided more long-term information. Most important, our adjusted estimate for long-term characteristics between patients with T2MI and T1MI may die beyond 1 year after the index event. Even after adjustment for their increased age and comorbidities, patients with T2MI remained at higher risk of long-term all-cause mortality compared with T1MI patients. Although previous meta-analyses suggested a true increase in odds of long-term mortality between patients with T1MI and T2MI, we were able to make the populations more comparable for future research evaluating the role of conventional ACS therapies (e.g., DAPT and coronary intervention) in patients with T2MI.

Short- and long-term mortality were high in patients with T2MI. Short- and long-term mortality were high in patients with T2MI, reflecting the increased risk of long-term all-cause mortality compared with T1MI. Although previous meta-analyses suggested a true increase in odds of long-term mortality between patients with T1MI and T2MI, we were able to make the populations more comparable for future research evaluating the role of conventional ACS therapies (e.g., DAPT and coronary intervention) in patients with T2MI.

The incidence of T2MI will likely escalate with the increasing use of high-sensitivity troponin assays. Although the detection of T2MI will likely enable the early treatment of this condition, it is not always recognized that severe myocardial ischemia, which can increase myocardial oxygen demand, might precipitate T2MI. Although clinicians may be aware that tachyarrhythmia can increase myocardial oxygen demand, they might not be aware that tachyarrhythmia might precipitate T2MI. Although the detection of T2MI will likely enable the early treatment of this condition, it is not always recognized that severe myocardial ischemia, which can increase myocardial oxygen demand, might precipitate T2MI. Although clinicians may be aware that tachyarrhythmia can increase myocardial oxygen demand, they might not be aware that tachyarrhythmia might precipitate T2MI. Therefore, our detection of T2MI may be enhanced, knowledge gaps concerning the optimal management of these patients will still need to be addressed. The incidence of T2MI will likely enable the early treatment of this condition, it is not always recognized that severe myocardial ischemia, which can increase myocardial oxygen demand, might precipitate T2MI. Although clinicians may be aware that tachyarrhythmia can increase myocardial oxygen demand, they might not be aware that tachyarrhythmia might precipitate T2MI. Therefore, our detection of T2MI may be enhanced, knowledge gaps concerning the optimal management of these patients will still need to be addressed.
### Table 2. Baseline characteristics of patients enrolled in RCTs and observational studies

|                       | RCT               | Observational studies | P values RCT vs observational studies |
|-----------------------|-------------------|-----------------------|---------------------------------------|
|                       | No. of studies (No. of patients) | 95% CI | No. of studies (No. of patients) | T1MI (95% CI) | T2MI (95% CI) | No. of studies (No. of patients) | P values T1MI vs T2MI |
| Age, y                | 62.1 (61.3-62.9)  | 51 (188,132)          | < 0.0001                              | 64.9 (65.0-68.9) | 14 (36,592) | 69.2 (66.1-72.4) | 15 (3930) | 0.02                        |
| Female, %             | 25.5 (24.0-27.1)  | 51 (188,132)          | < 0.0001                              | 29.8 (26.6-33.3) | 17 (38,352) | 44.2 (40.5-49.0) | 21 (4842) | < 0.0001                    |
| Diabetes mellitus, %  | 24.0 (22.0-26.1)  | 49 (142,096)          | 0.04                                  | 26.8 (23.3-30.7) | 17 (37,840) | 29.5 (25.5-33.9) | 18 (4771) | 0.05                        |
| Hypertension, %       | 63.3 (58.3-67.9)  | 45 (170,988)          | 0.32                                  | 67.1 (62.5-71.5) | 16 (35,276) | 69.9 (57.7-80.0) | 16 (8533) | 0.03                        |
| Prior MI, %           | 18.5 (15.0-22.5)  | 34 (147,006)          | 0.003                                 | 28.4 (25.2-31.8) | 11 (23,296) | 32.8 (25.9-40.6) | 11 (2877) | 0.21                        |
| Heart failure, %      | 8.3 (4.7-14.2)    | 6 (27,556)            | 0.25                                  | 14.7 (7.2-27.9)  | 9 (32,619)  | 21.1 (13.7-31.0) | 9 (3331)  | 0.08                        |

CI, confidence interval; DAPT, dual antiplatelet; MI, myocardial infarction; RCT, randomized controlled trial; T1MI, type 1 myocardial infarction; T2MI, type 2 myocardial infarction.

### Table 3. Management and outcomes of patients

|                        | RCT               | Observational studies | P values RCT vs observational studies |
|-----------------------|-------------------|-----------------------|---------------------------------------|
|                       | No. of studies (No. of patients) | Weighted mean, % (95% CI) | No. of studies (No. of patients) | T1MI weighted mean, % (95% CI) | T2MI weighted mean, % (95% CI) | P values T1MI vs T2MI |
| In-hospital            | NA                | NA                    | NA                                   | 6 (19,480) | 74.2 (66.0-81.0) | 20.8 (4.1-34.2) | < 0.0001 | 0.09 (0.04-0.21) |
| initiation of         |                    |                       |                                       | 8 (35,795) | 82.9 (77.8-87.0) | 28.2 (18.5-40.4) | < 0.0001 | 0.28 (0.20-0.39) |
| PCI                   | 35 (83,466)       | 99.8 (99.7-99.9)      | < 0.0001                             | 36.9 (36,825) | 64.4 (52.8-74.6) | 10.3 (4.3-22.6) | < 0.0001 | 0.17 (9.1-32.7)  |
| Reinfarction          | 4 (5321)          | 99.8 (99.6-99.9)      | < 0.0001                             | 5 (5396)  | 9.8 (6.3-14.9)   | 6.4 (4.0-10.1)  | < 0.0001 | 0.002 (0.87-0.89) |
| Short-term mortality  | 12 (97,269)       | 99.8 (99.7-99.9)      | < 0.0001                             | 8 (7249)  | 7.1 (5.5-8.8)    | 15.6 (10.3-20.8) | 0.0006  | 1.86 (1.20-2.88) *         |
| Long-term mortality   | 4 (33,593)        | 3.6 (2.3-5.4)         | < 0.0001                             | 16 (46,947) | 11.3 (6.4-19.2)  | 27.7 (20.6-36.1) | < 0.0001 | 2.47 (2.06-2.96) *        |

CI, confidence interval; DAPT, dual antiplatelet therapy; NA, nonapplicable (due to randomized comparison of dual antiplatelet therapy vs placebo); PCI, percutaneous coronary intervention; RCT, randomized controlled trials; T1MI, type 1 myocardial infarction; T2MI, type 2 myocardial infarction.

* Unadjusted comparison.

† Adjusted comparison.
Unadjusted Comparison of Long-Term All-Cause Mortality

| Study name | Statistics for each study | Events/Total | Follow-up (years) | Odds ratio and 95% CI | Relative weight |
|------------|---------------------------|--------------|------------------|----------------------|----------------|
|            | Odds ratio | Lower limit | Upper limit | p-Value | T1MI | T2MI |            |            |
| Grensleide | 1.73       | 0.61        | 4.86       | 0.30      | 6 / 41 | 13 / 147 | 1.00 | 2.34 |
| Stein      | 3.34       | 2.17        | 5.13       | 0.00      | 30 / 127 | 231 / 2691 | 1.00 | 6.25 |
| Radovanovitch | 3.38    | 2.74        | 4.16       | 0.00      | 122 / 1091 | 498 / 13829 | 1.00 | 8.51 |
| Shah       | 3.08       | 2.40        | 3.96       | 0.00      | 159 / 429 | 187 / 1171 | 1.00 | 8.11 |
| Baron      | 2.10       | 1.85        | 2.39       | 0.00      | 347 / 1403 | 2361 / 17488 | 1.00 | 9.14 |
| Smilowitz  | 1.04       | 0.63        | 1.73       | 0.87      | 45 / 116 | 41 / 137 | 1.00 | 5.50 |
| Lopez-Cuenca | 1.81    | 1.12        | 2.91       | 0.02      | 27 / 117 | 102 / 707 | 1.00 | 5.78 |
| Arora      | 3.77       | 2.71        | 5.25       | 0.00      | 92 / 264 | 96 / 775 | 1.00 | 7.27 |
| Cediel     | 2.68       | 1.83        | 3.94       | 0.00      | 77 / 194 | 74 / 376 | 2.00 | 6.72 |
| Neumann    | 1.54       | 0.73        | 3.27       | 0.26      | 14 / 99 | 18 / 188 | 2.00 | 3.64 |
| Gonzalez   | 0.57       | 0.25        | 1.26       | 0.17      | 8 / 55 | 64 / 278 | 2.00 | 3.36 |
| Saaby      | 2.73       | 1.78        | 4.20       | 0.00      | 58 / 119 | 94 / 360 | 2.00 | 6.25 |
| Sandoval 2017 | 1.48    | 0.71        | 3.07       | 0.29      | 31 / 140 | 12 / 77 | 2.00 | 3.78 |
| Lambrecht  | 3.47       | 2.25        | 5.34       | 0.00      | 74 / 119 | 115 / 360 | 3.00 | 6.23 |
| Chapman    | 2.87       | 2.29        | 3.61       | 0.00      | 268 / 429 | 430 / 1171 | 5.00 | 8.32 |
| Raphael    | 3.58       | 3.01        | 4.26       | 0.00      | 769 / 1054 | 587 / 1365 | 5.50 | 8.81 |
| Overall    | 2.47       | 2.06        | 2.96       | 0.00      |            |            |            |            |

F: 33.8%

T1MI: Type 1 Myocardial Infarction
T2MI: Type 2 Myocardial Infarction

Figure 2. Unadjusted comparison of long-term all-cause mortality. CI, confidence interval; T1MI, type 1 myocardial infarction; T2MI, type 2 myocardial infarction.

Adjusted Comparison of Long-Term All-Cause Mortality

| Study name | Statistics for each study | Hazard ratio and 95% CI | Relative weights | Follow-up (years) |
|------------|---------------------------|-------------------------|------------------|------------------|
|            | HR | 95% CI | P-value | | |
| Baron      | 1.03 | 0.86 | 1.23 | 0.75 | 14.91 | 1 |
| Chapman    | 1.51 | 1.21 | 1.88 | 0.00 | 13.58 | 5 |
| Cediel     | 1.41 | 1.02 | 1.94 | 0.04 | 10.26 | 2 |
| Landes     | 2.08 | 1.14 | 3.80 | 0.02 | 4.79 | 1 |
| Lopez-Cuenca | 0.88 | 0.48 | 1.62 | 0.68 | 4.70 | 2 |
| Saaby      | 2.00 | 1.32 | 3.04 | 0.00 | 7.82 | 1 |
| Shah       | 1.62 | 1.29 | 2.03 | 0.00 | 13.32 | 1 |
| Arora      | 1.98 | 1.44 | 2.73 | 0.00 | 10.31 | 1 |
| Neumann    | 1.16 | 0.59 | 2.27 | 0.66 | 4.07 | 2 |
| Raphael    | 1.40 | 1.22 | 1.61 | 0.00 | 16.23 | 5 |
| Overall    | 1.45 | 1.25 | 1.69 | 0.00 |            |            |

F: 4.67%

T1MI: Type 1 Myocardial Infarction
T2MI: Type 2 Myocardial Infarction

Figure 3. Adjusted comparison of long-term all-cause mortality. CI, confidence interval; HR, hazard ratio; T1MI, type 1 myocardial infarction; T2MI, type 2 myocardial infarction.
Limitations

Our systematic reviews had a few noteworthy limitations. First, the lack of patient-level data precluded us from computing adjusted odds ratios for short-term/intermediate mortality and reinfarction. Second, our adjusted comparison of long-term mortality may still be flawed by residual confounders that may not have been accounted for in the individual studies. Third, we could not compare the risk of cardiovascular mortality in patients with T2MI with that of patients with T1MI because only 3 studies reported cardiovascular mortality.19,26,27 Fourth, because we excluded studies of myocardial injury after surgeries, our summary estimates of T2MI could not be extrapolated to patients with postoperative T2MI. Finally, it was possible that some patients with T2MI might have only myocardial injury without actual myocardial necrosis. Because patients with myocardial injury generally had better outcomes than patients with myocardial infarction,79,81 our evaluations of odds of mortality may be underestimated because of the potential inclusion of patients with myocardial injury.

Conclusion

Even after accounting for their increased comorbidities, patients with T2MI still have higher all-cause long-term mortality compared with patients with T1MI. The efficacy, effectiveness, and safety of DAPT in T2MI have not been formally appraised in any RCTs or observational study. Therefore, the role of DAPT in T2MI remains undefined. This knowledge gap underscores the need for future studies evaluating DAPT in patients with T2MI to optimize the management of these high-risk patients.

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Table 4. Triggers of type 2 myocardial infarction

| Triggers of type 2 myocardial infarction | No. of studies (No. of patients) | Weighed mean, % (95% CIs) |
|------------------------------------------|---------------------------------|--------------------------|
| Arrhythmia                               | 9 (36,592)                      | 22.4 (16.1-30.3)         |
| Anemia/bleeding                          | 8 (35,044)                      | 15.9 (11.6-21.4)         |
| Respiratory diseases                     | 5 (12,682)                      | 13.7 (8.3-21.8)          |
| Heart failure                            | 4 (25,066)                      | 13.7 (8.3-21.8)          |
| Hypertensive crisis                      | 6 (11,204)                      | 11.5 (6.6-19.2)          |
| Sepsis/infection                         | 5 (24,387)                      | 10.1 (5.2-18.8)          |

CI, confidence interval.
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Supplementary Material
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