What is the optimal treatment for symptomatic patients with isolated coronary myocardial bridge? A systematic review and pooled analysis

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Background Myocardial bridging is a common coronary anomaly, with few severe adverse events but a relevant symptom burden. Myocardial bridging treatment, however, remains uncertain because of the lack of randomized trials.

Material MEDLINE/PubMed was systematically screened for studies reporting on isolated myocardial bridging diagnosed at coronary angiography or with coronary computed tomography in patients admitted for suspected angina or with an acute coronary syndrome. Baseline, treatment and outcome data were appraised and pooled according to treatment (medical therapy, bypass surgery/myotomy or stenting).

Results A total of 899 patients in 18 studies were included with a low prevalence of traditional risk factors, especially diabetes (15.6%, interquartile range 2.5–21.5). After a median of 31.0 months (interquartile range 12.4–37.1), major cardiovascular events (composite of death, myocardial infarction or target vessel revascularization) occurred in only 3.4% of the study patients and 78.7% (70.5–86.9; 95% confidence intervals (CI)) were managed conservatively and free of symptoms. When an invasive strategy was planned, freedom from angina was higher in patients treated with surgery [84.5% (78.4–90.7; 95% CI)] than in those treated with stenting [54.7% (38.9–70.6; 95% CI)]. Patients in the stenting group experienced a high incidence of major cardiovascular events related to target vessel revascularization [40.07% (19.83–60.32; 95% CI)].

Meta-regression showed that patients treated with beta-blockers or with a history of hypertension were more likely to remain free from angina (B = −0.6, P = 0.013; B = −0.66, P = 0.006).

Conclusion Patients with symptomatic isolated myocardial bridging generally have a good long-term prognosis. Pharmacological treatment alone, especially with beta-blockers, is able to improve angina in most cases. Surgical treatment appears to be more effective than stenting in nonresponders.

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Keywords: coronary artery bypass graft, congenital anomaly, myocardial bridge, myotomy, stenting

Introduction Myocardial bridging is anatomically defined as an intramural segment of a major epicardial coronary artery entrapped into cardiac muscle. It is the most common congenital anomaly of the coronary arteries, with a prevalence between 1.5 and 16% as assessed by coronary computed tomography (CT) and up to 80% at autopsy. Although most of these complications are infrequent, myocardial bridging therapy remains unclear because of the lack of randomized data. This is especially worrisome in the presence of recurrent angina despite optimal medical therapy. Beta-blockers usually are the first line of treatment in symptomatic patients, whereas surgical interventions such as myotomy (unroofing) or bypass surgery or coronary stenting are considered a second line option. In the absence of randomized controlled trials, definite evidence is still lacking and is limited to a small

arrhythmias,10 left ventricle (LV) dysfunction,11 apical ballooning syndrome and even sudden cardiac death.12–16
number of studies enrolling a limited number of patients with short-term follow-up.

The purpose of our study was to perform a meta-analysis of the available evidence to critically appraise clinical management and outcome events in patients suffering from myocardial bridging.

Methods

The current research was elaborated according to current guidelines, including the recent Preferred Reporting Items for Systematic reviews and Meta-Analyses amendment and recommendations from The Cochrane Collaboration and Meta-analysis Of Observational Studies in Epidemiology (MOOSE).18,19 English language restriction was applied. Search strategy and protocol were published and available on web (http://www.cardiogroup.org/protocols).

Search strategy and study selection

Pertinent articles were searched in Medline, Cochrane Library, Biomed Central and Google Scholar in keeping with established methods20 with Mesh strategy and with terms related to patients admitted with a diagnosis of suspected angina or acute coronary artery disease (CAD) (ACS): (myocardial OR intramyocardial) AND (bridging OR bridge OR milking) AND (stent+ OR ptca OR angioplasty) OR cabg OR bypass AND (graft+ OR surgery). Studies appraising only patients with myocardial bridging as well as studies including patients with and without myocardial bridging were included.

Two independent reviewers (E.C. and F.D.) first screened retrieved citations at the title and/or abstract level, with divergences resolved after consensus. If potentially pertinent, they were then appraised as complete reports according to the following explicit selection criteria. Studies were included if investigating patients with: first, an invasive or noninvasive (CT) angiographic diagnosis of myocardial bridging, defined as a systolic compression at least at least 50% of one or more segments of a coronary artery; second, presenting with suspected angina or ACS; and third, at least 18 years of age. Exclusion criteria were nonhuman setting, duplicate reporting (in which case the article reporting the largest sample of patients with myocardial bridging was selected), studies reporting also asymptomatic patients with incidental myocardial bridging finding and single case reports or studies not reporting follow-up of patients. Patients with prior history of obstructive CAD or coronary revascularization or with obstructive CAD were excluded to avoid CAD-related events.

Data extraction

The following data were abstracted on prespecified forms: authors, journal and year of publication, location of the study group, baseline features, localization and extension of myocardial bridging, treatment of choice [medical vs. PCI (percutaneous coronary intervention) vs. surgery both myotomy or coronary artery bypass graft (CABG)]. End-points of interest were death, myocardial infarction (MI), revascularization, rehospitalization, recurrence of chest pain vs. symptoms relief and complications related to surgery/PCI approach.

Internal validity and quality appraisal

Unblinded independent reviewers (E.C. and F.D.) evaluated quality of included studies on prespecified forms. To take into account the specific features of included studies,21 we modified the MOOSE items to separately abstract and appraise the study design, setting, data source, as well as risk of analytical, selection, adjudication, detection and attrition bias (expressed as low, moderate or high risk of bias, as well as incomplete reporting leading to inability to ascertain the underlying risk of bias). Moreover, we awarded overall credibility of studies included to summarized previous features. Zero points were assigned for retrospective design and one center study, one for prospective arrangement and two for a multicenter design. Moreover, two points were ascribed for low risk of bias, one for moderate risk and zero for high risk or unclear. If the sum of these scores was 10, a very high credibility was granted; if it was between seven and nine, high; four and six, moderate; one and three; low and zero, very low.

For the quality assessment of the selected studies, we used the Newcastle–Ottawa Scale for Assessing the Quality of Nonrandomized Studies in Meta-Analysis.20

Data analysis and synthesis

Continuous variables are reported as median and interquartile range (IQR). Categorical variables are expressed as n/N (%). Statistical pooling was performed with random-effect models with generic inverse-variance weighting and computing risk estimates with 95% confidence intervals (CIs), using RevMan 5.3 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark). Small study bias was appraised by graphical inspection of funnel plots. Standard hypothesis testing was set at the two-tailed 0.05 level.

Results

A total of 322 citations were first screened and appraised at abstract level; 24 articles were selected, among which three were excluded because those were investigating only baseline features without reporting outcome and/or follow-up,22–25 one as it also included asymptomatic patients26 and one because it was available only in the Chinese language.27 Finally, 18 studies were included in our review28–45 (Fig. 1, review profile).

The methodological and quality assessment was reported in Table A (see Supplementary material online, Appendix, http://links.lww.com/JCM/A108), showing an overall average quality of the selected studies, most of them being retrospective, single center and with acceptable...
risk of analyzed bias. Moreover, for each study, definitions of events and single follow-up were evaluated: patient status was obtained at an outpatient clinic examination or by telephonic interview registering major cardiovascular events (MACEs), symptoms of angina pectoris and ongoing antianginal treatment. Follow-up angiography was performed in four studies in a percentage of patients ranging from 20 to 100%. Myocardial bridging was defined as an intramyocardial systolic compression or milking of a segment of an epicardial coronary artery and identified in all studies performing angiography except in two in which patients underwent a 64-slice CT scan.\textsuperscript{33,34} In almost all studies, the presence of significantly coronary disease was an exclusion criteria (Table 1). Only eight studies reported the assessment of an ischemia stress test to relate symptoms to myocardial bridging.

Studies reported long-term follow-up of symptomatic patients with at least one myocardial bridging coronary segment were as follows: treated with medical therapy (seven studies with 702 patients), surgical treatment (CABG or myotomy, seven studies and 147 patients) or angioplasty with stenting (four studies, 54 patients).

A total of 899 patients with symptomatic myocardial bridging were included. Median age was 52.1 (IQR 50.0–55.9) years, most of the patients were men (median 73.0%; IQR 66.2–75.7) showing at pooled analysis an overall average incidence of traditional cardiovascular risk factors with low prevalence of diabetes (Table 2).

At admission, most patients presented anginal symptoms [typical angina, median 93.84% (IQR 46.7–100.0)] whereas dyspnea and acute MI were less frequently reported (Table 3).

Myocardial bridging involved 910 coronary segments in 899 patients and were mainly located in the middle-part of the left descending artery (Table 4).

Pharmacological therapy mainly consisted of beta-blockers (51.65%; IQR 30.73–79.06) and calcium channel blocker (33.13%; IQR 27.96–56.09). Some studies also reported prescription of nitrates (19.64%; IQR 13.94–28.17).\textsuperscript{29,30,33,42}

The overall median follow-up was 31.0 months (IQR 13.8–37.2). At the pooled analysis, the overall percentage of patients’ freedom of angina was 75.7% (70.9–80.4; 95% CI), with a higher relief of symptoms with surgical treatment [84.6% (78.4–90.7; 95% CI)] as compared with stent angioplasty [54.7% (38.9–70.6; 95% CI)] (Fig. 2).

Yet, patients in the medical therapy group demonstrated an overall percentage of freedom of angina equal to 78.7% (70.5–86.9; 95% CI). MACE occurred at a low rate (30, 3.3%). Death was registered in six patients: five in medical therapy group (two due to a sudden event, three were heart failure-related) and one in the stenting group due to a MI. MI, death or other major in-hospital complications were not reported in the surgical group. None of the patients in this group sustained a MI or other major adverse cardiac events during follow-up. One patient, initially treated by myotomy, underwent coronary artery bypass surgery due to recurrent angina with angiographic demonstration of residual narrowing in the left anterior descending.

Patients in the PCI group experienced a high incidence of MACE related to target vessel revascularization, as
<table>
<thead>
<tr>
<th>First author (year of publication)</th>
<th>Journal</th>
<th>Sample size (number of patients with MB)</th>
<th>Imaging technique</th>
<th>Definition of MB</th>
<th>Patients with presence of concomitant CAD or other cardiac diseases</th>
<th>Ischemia assessment (myocardial SPECT and/or ECG stress test)</th>
<th>Treatment</th>
<th>Follow-up modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Çiçek (2011)</td>
<td>Card Rev Medicine</td>
<td>118</td>
<td>Angiography</td>
<td>Systolic narrowing of an epicardial artery, evaluated in percentages</td>
<td>Excluded</td>
<td>Yes</td>
<td>Medical therapy</td>
<td>The prognosis and cardiac events were observed from the patients' file and phone calls with patients</td>
</tr>
<tr>
<td>Juillère (1995)</td>
<td>Am Heart J</td>
<td>28</td>
<td>Angiography</td>
<td>Systolic reduction of the arterial lumen assessed visually evaluated in percentage</td>
<td>Excluded</td>
<td>Not reported</td>
<td>Medical therapy</td>
<td>Follow-up data were obtained by means of a detailed questionnaire sent to all presumably living patients</td>
</tr>
<tr>
<td>Kim (2010)</td>
<td>Circ J</td>
<td>308</td>
<td>Angiography</td>
<td>Tramyocardial systolic compression or milking of a segment of an epicardial coronary artery. Intracoronary nitroglycerin was administered once MB was suspected during CAG</td>
<td>Excluded</td>
<td>Yes</td>
<td>Medical therapy</td>
<td>Follow-up data were obtained from direct telephone contact and hospital and computer records. Review of all available medical records was performed for in-hospital and late outcomes</td>
</tr>
<tr>
<td>Ural (2009)</td>
<td>Clin Cardiol</td>
<td>59</td>
<td>Angiography</td>
<td>More than 70% narrowing in the LAD during systole. Quantitative analysis was performed by 2 trained observers</td>
<td>Excluded</td>
<td>Not reported</td>
<td>Medical therapy</td>
<td>Follow-up was carried out by physical examination, echocardiography, treadmill exercise test and/or myocardial perfusion scintigraphy</td>
</tr>
<tr>
<td>Marcos-Alberca (2011)</td>
<td>Int J Cardiol</td>
<td>31</td>
<td>noninvasive coronary angiography with 64-MDCT</td>
<td>Coronary angiography with MDCT was performed using a 64-slice scanner with retrospective ECG gating (Brilliance 64; Philips Medical Systems, RK Philips, Eindhoven, The Netherlands). Performance, interpretation and reporting of MDCT accomplished the recommendations of the Society of Cardiovascular Computed Tomography. Myocardial bridging was diagnosed when an epicardial artery segment was partially or totally covered by myocardial tissue. Partially encased myocardial bridge was defined when arterial segment myocardium cover was &lt;180° and total encased myocardial bridge if the arterial segment was surrounded &gt;180° by myocardium in cross-sectional images</td>
<td>Excluded</td>
<td>Not reported</td>
<td>Medical therapy</td>
<td>Patient status was obtained at an outpatient clinic or by telephonic interview. All patients (100%) were contacted and asked about the advent of any event after the MDCT scan. Major adverse clinical events, symptoms of angina pectoris and ongoing antianginal treatment were assessed</td>
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</table>
### Table 1 (continued)

<table>
<thead>
<tr>
<th>First author (year of publication)</th>
<th>Journal</th>
<th>Sample size (number of patients with MB)</th>
<th>Imaging technique</th>
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<th>Follow-up modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubinshtein (2013)</td>
<td>Eur Heart J Cardiovasc Imaging</td>
<td>117</td>
<td>Noninvasive coronary angiography with 64-MDCT</td>
<td>CCTA was performed using a 64-channel scanner (Brilliance 64; Philips Healthcare, Cleveland, Ohio, USA), with retrospective ECG gating. CCTA were analyzed using a number of available methods, including axial views, cross-sectional imaging (double oblique) and multiplanar reformation. MB was diagnosed when a segment of an epicardial coronary artery took an intramyocardial course causing it to be covered by a bridge of myocardium</td>
<td>Excluded</td>
<td>Not reported</td>
<td>Medical therapy</td>
<td>Patients were followed for a mean duration of 6.1 ± 1 years. Retrospective analysis of electronic records of hospitalizations and mortality was undertaken at the end of the study period</td>
</tr>
<tr>
<td>Lozano (2002)</td>
<td>Rev Esp Cardiol</td>
<td>35</td>
<td>Angiography</td>
<td>Existence of systolic compression of the anterior descending coronary artery that produced more than 50% stenosis of the arterial lumen, confirmed by manual measurements or quantitative analysis, depending on the capacity of the laboratory at the time of the study</td>
<td>Excluded</td>
<td>Not reported</td>
<td>Medical therapy</td>
<td>Follow-up was carried out by telephone and completed with a review of the medical histories of the patients who had new admissions and medical records at one of the hospitals where the study was made. The clinical situation of patients, medical treatment at time of follow-up and events experienced (death, myocardial infarction, need to repeat coronary angiography or revascularization) were analyzed for the follow-up period</td>
</tr>
<tr>
<td>Sun (2012)</td>
<td>JCS</td>
<td>13</td>
<td>Angiography</td>
<td>Myocardial bridging of the left anterior descending artery</td>
<td>Excluded</td>
<td>Not reported</td>
<td>CABG</td>
<td>Survivors were contacted by letter and telephone</td>
</tr>
<tr>
<td>Wan (2005)</td>
<td>Interact Cardiovasc Thorac Surg</td>
<td>19</td>
<td>Angiography</td>
<td>Systolic compression of coronary segment more than 55% during systole</td>
<td>Excluded</td>
<td>Yes</td>
<td>CABG or myotomy</td>
<td>All patients were contacted by letter and telephone. Symptoms of recurrent angina and CCS class status were assessed</td>
</tr>
<tr>
<td>Wu (2007)</td>
<td>Chin Med J</td>
<td>31</td>
<td>Angiography</td>
<td>Coronary artery lumen compression during evaluation with angiography</td>
<td>8 (25%) associated CAD, 9 (29%) with associated vascular or aortic disease</td>
<td>Not reported</td>
<td>CABG or myotomy</td>
<td>Clinical evaluation, follow-up angiography performed in 21 patients (88%)</td>
</tr>
<tr>
<td>First author (year of publication)</td>
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<td>Rezayat (2006)</td>
<td>Saudi Med J</td>
<td>26</td>
<td>Angiography</td>
<td>The diameter of the tunneled segment was measured by digital caliper in systole and diastole. The systolic reduction of intraluminal diameter was between 60 and 80%</td>
<td>6 (20%) with associated CAD, mitral valve disease in 1 patient</td>
<td>Yes</td>
<td>Myotomy</td>
<td>Clinical evaluation, follow-up angiography performed in 12 patients (41%)</td>
</tr>
<tr>
<td>Huang (2007)</td>
<td>Chin Med J (Eng)</td>
<td>11</td>
<td>Angiography</td>
<td>Systolic compression of the anterior descending coronary artery</td>
<td>Excluded</td>
<td>Not reported</td>
<td>CABG</td>
<td>Follow-up was carried out by telephone and completed with a review of the medical histories of the patients who had new admissions and medical records at the hospital. Clinical evaluation was also accomplished by direct interview of the patients at clinic visits</td>
</tr>
<tr>
<td>Haager (2000)</td>
<td>Heart</td>
<td>11</td>
<td>Angiography</td>
<td>Bridging of the central portion of the left anterior descending coronary artery in all the patients</td>
<td>Excluded</td>
<td>Yes</td>
<td>PTCA + BMS</td>
<td>At 2 years after stent implantation, a standardized questionnaire was administered, either by phone or at an outpatient clinic visit, to assess clinical symptoms, daily activities without chest pain or anginal symptoms, subjective symptom quality, objective CCS class status, any hospital admissions or physician visits for chest pain and current drug treatment. Follow-up angiography performed in all patients</td>
</tr>
</tbody>
</table>
### Table 1 (continued)

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<tr>
<th>First author (year of publication)</th>
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<th>Treatment</th>
<th>Follow-up modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kunarnnemi (2008) Catheter Cardiovasc Interv</td>
<td>12</td>
<td>Angiography</td>
<td>Significant myocardial bridging was defined as &gt;50% reduction in the lumen of an epicardial coronary artery in systole by a quantitative coronary analysis determined in two orthogonal projections</td>
<td>Excluded</td>
<td>Yes</td>
<td>PTCA, 67% DES</td>
<td>The patients were contacted periodically (3–6 months) over phone and their compliance with medical therapy was assessed along with the incidence of symptom recurrence or cardiac events. Follow-up angiography performed in 6 patients (20%)</td>
<td></td>
</tr>
<tr>
<td>Kursakiuli (2004) Japan H J</td>
<td>12</td>
<td>Angiography</td>
<td>Quantitative measurements were done from digital images with dedicated software (Quantacor; QCA, Siemens; Erlangen, Germany)</td>
<td>Excluded</td>
<td>Not reported</td>
<td>PTCA + BMS</td>
<td>Interviewed in person or by phone by their primary physician with respect to clinical symptoms. Follow-up angiography performed in all patients</td>
<td></td>
</tr>
<tr>
<td>Bockeria (2013) J Card Surg</td>
<td>39</td>
<td>Angiography</td>
<td>&gt;50% systolic compression in proximal LAD</td>
<td>Atherosclerosis &gt;40%, myotomy/ stenting</td>
<td>Yes</td>
<td>CABG or myotomy</td>
<td>All patients underwent follow-up coronary angiography</td>
<td></td>
</tr>
<tr>
<td>Iversen (1992) Scand J Thor Cardiovasc Surg</td>
<td>18</td>
<td>Angiography</td>
<td>&gt;75% at rest or using isoproterenol</td>
<td>Excluded</td>
<td>Not reported</td>
<td>CABG or myotomy</td>
<td>Postoperative treadmill tests in all cases and postoperative myocardial thallium scans at rest and under isoproterenol stimulation. Repeated coronary angiography performed in three patients</td>
<td></td>
</tr>
<tr>
<td>Ernst (2013) the journal of invasive cardiology</td>
<td>15</td>
<td>Angiography</td>
<td>&gt;50% systolic, &gt;20% diastolic</td>
<td>Excluded</td>
<td>Yes</td>
<td>PTCA + DES</td>
<td>Clinical and noninvasive assessments of myocardial ischemia were determined every 6 months over 5 years and QCA was performed 12 and 24 months postprocedure if not urged differently by deterioration of clinical symptoms and/or presence of positive ischemia tests</td>
<td></td>
</tr>
</tbody>
</table>

BMS, bare metal stent; CABG, coronary artery bypass graft; CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; CCTA, cardiac computed tomography angiography; DES, drug eluting stent; LAD, left anterior descending; MB, myocardial bridging; MDTC, multidetector computed tomography; PTCA, percutaneous transluminal coronary angiography; SPECT, single-photon emission computed tomography.
observed in the forest plot [40.7% (19.83–60.32; 95% CI)] (Fig. 3).

A meta-regression was performed, showing a better outcome in terms of freedom from angina for patients treated with beta-blockers and in those with a history of hypertension ($R \ = \ -0.6; P = 0.013$ and $R = -0.66; P = 0.006$). No other significant differences or significant interaction were found even after performing a separate analysis for each treatment group (Fig. 4).

There was no systematic bias apparently as assessed by funnel plot inspection and with Egger’s test, which was non-significant (Fig. A, see Supplementary material online, http://links.lww.com/JCM/A110).

Discussion

The main findings of our meta-analysis are: first, patients with symptomatic isolated myocardial bridging and without obstructive CAD have a good long-term prognosis with a very low rate of adverse events; second, in the majority of patients, pharmaceutical treatment alone, especially with beta-blockers, is successful in relieving symptoms; and third, in patients in whom an invasive strategy is deemed as needed, surgical treatment appears to be more effective in controlling symptoms than stenting.

From its first description by Reyman in 1737, myocardial bridging provoked discussions about its implications in the development of angina. Traditionally, it was considered a benign condition, in part due to its frequency at autopsy in which, with various length and depth, it could be observed in as much as 80% of the general population. Moreover, as most of the coronary flow occurs during diastole, it has been suggested that a systolic impediment of flow can have a negligible effect on myocardial function.

The first angiographic description by Portmann and Iwig in 1960 documented the milking effect of the muscle bridge on the coronary flow during systole. However, coronary angiography has a limited diagnostic accuracy for myocardial bridging diagnosis (prevalence of 1.5–16%), increasing its sensitivity after nitroglycerine administration. The noninvasive 64-slice coronary CT scan has a higher diagnostic rate, ranging from 20 to 30% as different from angiography; it can identify the muscle lying on top of the coronary.

The clinical relevance of myocardial bridging is also unclear because of its high prevalence in the general population and the fact that myocardial bridging has been associated with different adverse clinical events, such as myocardial ischemia and acute coronary syndromes, coronary spasm, ventricular septal rupture, ventricular tachycardia, exercise-induced arrivoventricular conduction block, transient ventricular dysfunction, early death after cardiac transplantation and also sudden cardiac death.

Three mechanisms have then been proposed to explain the pathophysiological findings resulting from the presence of myocardial bridging. The first is that phasic systolic compression of the artery produces a persistent mid-to-late diastolic reduction in coronary artery diameter. Tachycardia that shortens the diastolic period and therefore, decreases coronary blood flow, might be an important factor in the pathogenesis of angina in patients.

### Table 4 Angiographic features

<table>
<thead>
<tr>
<th>Overall (n = 899; 18 studies)</th>
<th>910</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary segments involved</td>
<td>100.0 (86.7–100.0)</td>
</tr>
<tr>
<td>Site of myocardial bridging</td>
<td>28.8 (14.7–64.4)</td>
</tr>
<tr>
<td>Proximal</td>
<td>Medium</td>
</tr>
<tr>
<td>Left descending, n = 846</td>
<td>90.9 (73.8–100.0)</td>
</tr>
<tr>
<td>Circumflex, n = 32</td>
<td>10.8 (5–17.2)</td>
</tr>
<tr>
<td>Obtuse marginal</td>
<td>Ramus intermedus</td>
</tr>
<tr>
<td>3.4 (2.6–4.3)</td>
<td>2.4 (1.5–3.4)</td>
</tr>
</tbody>
</table>

Values are numbers or median of percentages with 25th and 75th percentiles.
with myocardial bridging. The second postulate is that milking may produce systolic retrograde flow and overall flow disruption with augmented shear stress. This is probably the basis for the characteristic development of atherosclerosis in the proximal portion of the myocardial bridging, whereas the bridged segment is usually free from atherosclerosis (atherosclerosis sparing). Third, myocardial bridging has been related with coronary endothelial dysfunction that is an early stage of atherosclerosis and is associated with spasm, symptoms and adverse events.

Therapeutic approaches arise from these mechanisms. Beta-blocker and calcium channel blockers increase diastolic coronary flow by decreasing tachycardia and are preferred as first line of treatment in symptomatic patients. However, these agents have not been studied in randomized controlled trials. On the other hand, nitrates should probably be avoided as they could increase the angiographic degree of systolic narrowing due to the reduced systolic pressure and vasodilation. Finally, invasive treatment with percutaneous stenting or surgery (either myotomy or bypass surgery) should be limited to patients with severe symptoms that persist despite optimal medical treatment.

Our meta-analysis shows that medical treatment is highly effective in reducing symptoms, whereas coronary stenting had a lower efficacy than surgery. Consequently, our data strengthen the assumption that stent implantation should not be considered as the preferred treatment due to its high restenosis rate. Stenting in the selected studies was frequently complicated by neointimal proliferation, thrombus formation and stent compression (or even fracture) leading to high restenosis rate in the bare metal stent era. Intravascular ultrasonography will therefore be beneficial to verify optimal stent expansion.

Surgical treatment (especially ‘unroofing’) appears to be the most useful option for symptom control in selected patients, but the choice of the technique depends on myocardial bridging characteristics and local experience. Supra-arterial debridging myotomy is performed...
Fig. 3

Forest plots for target vessel revascularization in percutaneous transluminal coronary angioplasty group.

Concerning the assessment of myocardial bridging inducing myocardial ischemia, it has been suggested that stress single PET (single-photon emission computed tomography) can detect reversible myocardial perfusion defects in patients with myocardial bridging and relate the amount of ischemia to the degree of systolic luminal narrowing.\(^6\)\(^1\) Moreover, dipyridamole stress single-photon emission computed tomography imaging showed good agreement with exercise stress single-photon emission computed tomography imaging (\(k = 0.765\) for the detection of ischemia in patients with myocardial bridging.\(^6\)\(^2\) In spite of these, half of the studies included in our analysis reported the assessment of myocardial ischemia in the myocardial bridging territory. Of note, preangiography myocardial bridging assessment is as important as difficult is its invasive assessment, due to available physiology techniques such as fractional flow reserve. Fractional flow reserve theory applies only during maximum hyperemia, when all resistances are constant and the derivation of flow reserve from pressure is possible. However, the cyclic nature of the lumen compression in myocardial bridging creates variable nonlinear interactions between pressure-loss and flow, ultimately invalidating the technique for myocardial bridging assessment.\(^1\)\(^3\)\(^1\)\(^7\) Some studies have reported the use of diastolic Fractional Flow Reserve as a better index for this purpose\(^6\)\(^3\) and phasic pressure indices focused on the diastole as the instantaneous wave-free ratio might lead to better results. In addition, others have stressed the importance of positive inotropic agents such as dobutamine to better evaluate the hemodynamic consequences of the myocardial bridging.\(^3\)\(^6\)\(^4\) Nevertheless, the limited sample of the abovementioned studies limits the clinical use of such diagnostic techniques. We may conclude that, although medical therapy appears to be superior to coronary stenting, ischemia-guided revascularization may be considered on a case-by-case basis for asymptomatic patients with refractory symptoms to maximal medical therapy and who are not optimal surgical candidates.

Our meta-regression analysis exhibited that patients with a history of hypertensive disease seem to have a greater benefit from medical therapy. This finding could be in part explained by the fact that hypertrophic remodeling of the LV might respond better to administration of beta-blockers by reducing vascular compression, increasing luminal diameter and normalizing blood flow velocities within the tunneled arterial segments as reported in myocardial bridging in presence of hypertrophic cardiomyopathy.\(^1\)\(^7\) Significantly, in a cohort of adult patients with hypertrophic cardiomyopathy, event rate was also not increased in those with myocardial bridging,\(^6\)\(^3\) strengthening our finding that myocardial bridging has a benign course in the majority of patients including those with exaggerated myocardial contraction such as in patients with hypertrophic cardiomyopathy.

**Study limitations**

Our work has several limitations. There are no universally accepted criteria for the diagnosis of myocardial bridging and studies included in the meta-analysis employed different definitions and diagnostic methods. Not every patient received intracoronary nitroglycerine at the time of angiography, thus the prevalence could be underestimated. Moreover, coronary CT angiography is a modality that is probably more accurate for anatomic diagnosis of myocardial bridging than invasive angiography revealing myocardial bridging in about a third of patients screened. However, coronary CT is usually performed in lower risk patients, hence introducing a large heterogeneity in the
We think that adding these studies to our analysis, despite the abovementioned limitation, better reflects the real clinical setting of myocardial bridging assessment.

We were not able to find a randomized controlled clinical myocardial bridging trial, but only prospective follow-up data of symptomatic patients with a diagnosis of myocardial bridging. Hence, conclusions derived from...
observational studies should be drawn cautiously due to inherent limitation of retrospective and observational data. However, our work constitutes the largest systematic effort to appraise myocardial bridging scientific data. Surgical series probably may suffer from a publication bias and only those with good long-term outcomes might be eventually published. Furthermore, comparing patients who received revascularization with the others may be misleading, as it seems reasonable that many patients were first selected for medical therapy and then revascularization was performed just for patients with refractory symptoms. This fact should stress the importance to start therapy with medical agents in clinical practice. Finally, the fact that myocardial ischemia was not systematically assessed is a limitation that may have altered the treatment's effect.

Conclusion
Myocardial bridge is a common finding (especially in coronary CT) and a possible cause of angina but an infrequent cause of MACE. Medical therapy with beta-blockers is the first line choice in symptomatic patients without concomitant obstructive CAD whereas surgical myotomy or CAGB should be limited to selected patients who experience significant symptoms despite drugs. Angioplasty with stenting should probably be avoided in most cases due to the high frequency of repeated revascularization reported in this group of patients.

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Conflicts of interest
There are no conflicts of interest.

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