Mini-Review: Current Perspective

Update on Myocardial Bridging

Stefan Möhlenkamp, MD; Waldemar Hort, MD; Junbo Ge, MD; Raimund Erbel, MD

Muscle overlying the intramyocardial segment of an epicardial coronary artery, first mentioned by Reymann1 in 1737, is termed a myocardial bridge, and the artery coursing within the myocardium is called a tunneled artery (Figure 1). It is characterized by systolic compression of the tunneled segment, which remains clinically silent in the vast majority of cases. An in-depth analysis of autopsy samples was first presented by Geiringer et al in 1951, but clinical interest and systematic research was triggered by an observed association of myocardial bridging with myocardial ischemia.2-5

New imaging techniques have led to improved identification and functional quantitation of myocardial bridging in vivo, which is crucial for establishing a link between systolic compression and the clinical presentation, and hence for commencing appropriate therapy. In the present article, we summarize clinically relevant aspects of myocardial bridging with an emphasis on morphological and hemodynamic alterations and their representation in imaging techniques.

Prevalence

The prevalence varies substantially among studies with a much higher rate at autopsy versus angiography (Table).2-4,28 Variation at autopsy may in part be attributable to the care taken at preparation and the selection of hearts. Poláček, who included myocardial loops, reports the highest rate with bridges or loops in 86% of cases.29 On average, myocardial bridges are present in about one third of adults.

The rate of angiographic bridging is <5%, attributable to thin bridges causing little compression. In subjects with angiographically normal coronary arteries, the use of provocation tests may enhance systolic myocardial compression and thereby reveal myocardial bridges in ≤40% of cases.26,30

A high prevalence has also been reported in heart transplant recipients33 and in patients with hypertrophic obstructive cardiomyopathy (HOCM).31 In the latter, more rigorous contraction may unmask otherwise undetectable bridges. Myocardial bridging may be found at multiple sites in HOCM,32 but also in patients without.33 De novo, previously nonexistent myocardial bridging has been suggested for both transplanted hearts34 and HOCM,35 but conclusive proof is lacking.36

Comparative Anatomy

An epicardial course of coronary arteries is not obligatory in mammals. In rodents and lagomorpha, the major vessels are embedded in myocardium beneath the epicardial surface (Type I).5,29 Animals with a predominantly epicardial course of coronary arteries (Type II) include small ruminants, carnivores, and primates.29,37 Whereas the major coronary arteries in the gorilla form an epicardial network, they tend to take a mural course in the chimpanzee.36 In goats and sheep, bridges are more frequent than in humans.8 They can also be observed in canines, felines, and seals.37 In some mammals they are missing or extremely rare, such as in horses and pigs (Type III).29 Myocardial bridges are congenital in origin38-40 and likely reflect an evolutionary remnant in the genetic code.

Morphology

Myocardial bridges are most commonly localized in the middle segment of the left anterior descending coronary artery (LAD).29 In the presence of two parallel LAD branches, one frequently takes an intramural course.2 Diagonal and marginal branches may be involved in 18% and 40% of cases, respectively.8,36 Angiographically, myocardial bridges are almost exclusively spotted in the LAD. They are located at a depth of 1 to 10 mm10,41 with a typical length of ∼10 to 30 mm.3 Deformation is predominantly eccentric,5 as confirmed by intravascular ultrasound (IVUS)-based studies.42 Occasionally, the arteries may take a very deep course through the septum approaching the right ventricular subendocardium (Figure 2).

Ferreira et al12 distinguished between two types of bridging: (1) superficial bridges (75% of cases) crossing the artery perpendicularly or at an acute angle toward the apex, and (2) muscle bundles arising from the right ventricular apical trabeculae (25% of cases) that cross the LAD transversely, obliquely, or helically before terminating in the interventricular septum. Arterial segments may also be located in a deep interventricular gorse. Such “incomplete” bridges may appear during adulthood in concomitant disease,2 in which a segment is compressed during systole although its surface is not fully covered by myocardial fibers, but by a thin layer of connective tissue, nerves, and fatty tissue.36

Myocardial loops derive from atrial myocardium, surround the vessel three quarters of the circumference, and return to

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atrial myocardium. They are usually thinner compared with LAD bridges (0.1 to 0.3 mm) and have a width of 10 to 15 mm (range 2 to 30 mm). Occasionally, a bridge may involve a coronary vein. However, myocardial loops and venous bridges appear to have no clinical relevance.

**Presence and Absence of Atherosclerosis in Relation to Myocardial Bridging**

Coronary atherosclerosis in association with myocardial bridging has primarily been studied in the LAD. The segment proximal to the bridge frequently shows atherosclerotic plaque formation, although the tunneled segment is typically spared (Figures 3 and 4). This is supported by studies on a cellular and ultrastructural level. In contrast to proximal and distal segments, foam cells and modified smooth muscle cells were missing in patients’ tunneled segments. Extramural, epicardial segments in cholesterol-fed rabbits developed intimal atherosclerosis with accumulation of ApoB and proliferating cell nuclear antigens (PCNA) in smooth muscle cells of the intima. These changes were not seen in any arterial wall component in tunneled segments. Furthermore, endothelial cell permeability was increased both in atherosclerotic and nonatherosclerotic portions of epicardial segments in high-cholesterol rabbits but not in tunneled segments or in normal control arteries.

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**Prevalence of Myocardial Bridging at Autopsy and Angiography**

<table>
<thead>
<tr>
<th>Author (Reference No.)</th>
<th>Sample Size, n</th>
<th>With Bridges, %</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Autopsy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geiringer²</td>
<td>100</td>
<td>23</td>
<td>LAD</td>
</tr>
<tr>
<td>Edwards et al⁶</td>
<td>276</td>
<td>5</td>
<td>All coronaries, 87% in the LAD</td>
</tr>
<tr>
<td>Poláček²</td>
<td>70</td>
<td>86</td>
<td>Including RCA loops, LAD: 60%</td>
</tr>
<tr>
<td>Giampalmo et al⁸</td>
<td>560</td>
<td>7</td>
<td>All coronaries, 95% LAD only</td>
</tr>
<tr>
<td>Lee and Wu⁹</td>
<td>138</td>
<td>58</td>
<td>LAD</td>
</tr>
<tr>
<td>Penther et al¹⁰</td>
<td>187</td>
<td>18</td>
<td>LAD</td>
</tr>
<tr>
<td>Risse and Weiler¹¹</td>
<td>1056</td>
<td>26</td>
<td>All coronaries, 88% in the LAD</td>
</tr>
<tr>
<td>Ferreira et al¹²</td>
<td>90</td>
<td>56</td>
<td>All coronaries</td>
</tr>
<tr>
<td>Baptista and DiDio¹³</td>
<td>82</td>
<td>54</td>
<td>All coronaries, 35% in the LAD</td>
</tr>
<tr>
<td>Ortale et al¹⁴</td>
<td>37</td>
<td>56</td>
<td>LAD (7% coronary veins with bridges)</td>
</tr>
<tr>
<td>Kosinski and Grzybiak¹⁵</td>
<td>100</td>
<td>41</td>
<td>All coronaries</td>
</tr>
<tr>
<td><strong>Angiography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noble et al¹⁴</td>
<td>5250</td>
<td>0.5</td>
<td>All patients</td>
</tr>
<tr>
<td>Binet et al¹⁶</td>
<td>700</td>
<td>0.7</td>
<td>Unspecified series of patients</td>
</tr>
<tr>
<td>Ishimori et al¹⁷</td>
<td>313</td>
<td>1.6</td>
<td>All patients, systolic compression ≥50%</td>
</tr>
<tr>
<td>Greenspan et al¹⁸</td>
<td>1600</td>
<td>0.9</td>
<td>All patients, exclusion of associated disease</td>
</tr>
<tr>
<td>Rossi et al¹⁹</td>
<td>1146</td>
<td>4.5</td>
<td>All patients</td>
</tr>
<tr>
<td>Voß et al²⁰</td>
<td>848</td>
<td>2.5</td>
<td>All patients</td>
</tr>
<tr>
<td>Kramer et al²¹</td>
<td>658</td>
<td>12</td>
<td>Patients with otherwise normal angiograms</td>
</tr>
<tr>
<td>Angelini et al⁶</td>
<td>1100</td>
<td>4.5</td>
<td>All patients</td>
</tr>
<tr>
<td>Garcia et al²²</td>
<td>936</td>
<td>4.9</td>
<td>All patients</td>
</tr>
<tr>
<td>Wymore et al²³</td>
<td>64</td>
<td>33</td>
<td>Heart transplantation patients</td>
</tr>
<tr>
<td>Somanath et al²⁴</td>
<td>1500</td>
<td>1.1</td>
<td>All patients</td>
</tr>
<tr>
<td>Gallet et al²⁵</td>
<td>1920</td>
<td>1.0</td>
<td>LAD only (13 of 19 patients with an isolated bridge)</td>
</tr>
<tr>
<td>Diefenbach et al²⁶</td>
<td>1780</td>
<td>3.5</td>
<td>All patients</td>
</tr>
<tr>
<td>Among those:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Juillière et al²⁷</td>
<td>7467</td>
<td>0.8</td>
<td>All patients</td>
</tr>
<tr>
<td>Harikrishnan et al²⁸</td>
<td>3200</td>
<td>0.6</td>
<td>All patients</td>
</tr>
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</table>
Mechanisms for Atherosclerosis in the Segment Proximal to the Bridge

Hemodynamic forces may explain atherosclerotic plaque formation at the entrance to the tunneled segment. There, the endothelium is flat, polygonal, and polymorph, indicating low shear, whereas in the tunneled segment, the endothelium has a helical, spindle-shaped orientation along the course of the segment as a sign of laminar flow and high shear. Low shear stress may induce the release of endothelial vasoactive agents such as endothelial nitric oxide synthase (eNOS), endothelin-1 (ET-1), and angiotensin-converting enzyme (ACE). Their levels were significantly higher in proximal and distal segments compared with the tunneled segment. Thus, low shear stress may contribute to atherosclerotic plaque formation proximal to the bridge, whereas high shear stress may have a protective role within the tunneled segment. In addition, an increase in local wall tension and stretch may induce endothelial injury and plaque fissuring with subsequent thrombus formation in the proximal segment, which is supported by autopsy and clinical observations.

Mechanisms for Ischemia

Neither nonsignificant stenosis proximal to the bridge nor systolic compression of the tunneled segment alone can sufficiently explain severe ischemia and associated symptoms. Experimental LCX occlusion, initially during systole only and then during continuing occlusion extending increasingly into diastole, resulted in distinct shortening of inflow time with significant reduction of epicardial flow, subendocardial flow, and distal coronary pressure. After releasing the occlusion, diastolic flow increased in correspondence with an increasing duration of vessel occlusion, despite a decrease in mean flow. This increased diastolic/systolic flow ratio was later verified in patients. Consistent with clinical findings, the increase in diastolic flow could not fully compensate for the decrease in mean flow resulting in reduced coronary flow reserve, which could not be explained by impaired vasodilatory capacity of resistance vessel.

When arterial occlusion was limited to systole, phasic coronary blood flow and distal coronary pressure was observed to resume with considerable delay contributing to reduced myocardial oxygen consumption and increased coronary sinus lactate concentration. This delayed diastolic relaxation was later identified in humans as an important mechanism contributing to ischemia with frame-by-frame analysis of IVUS images.

With the use of simultaneous proximal and distal pressure recordings, Ge et al identified the highest intravascular pressure just proximal to the bridge and a pressure gradient across the bridge. A distinct negative pressure in late diastole was preceded by a pressure peak beneath the bridge. Klues et al observed the highest systolic pressure within the tunneled segment but found no pressure gradient across the bridge. All their patients had significant tortuosity of the tunneled segment at the entry and exit sites. The central pressure chamber was interpreted as a result of heterogeneous compression of the tunneled segment with higher proximal and distal forces compared with the central portion, potentially contributing to reduced coronary flow reserve.

The likelihood of ischemia also increases with the intramycocardial depth of the tunneled segment: In 22 of 39 hearts, historical cross section showing a tunneled segment and a tunneal branch of the LAD. The epicardial segment shows intima thickening as a sign of early atherosclerosis but the tunneled segment does not.
myocardial fibrosis and contraction band necrosis were detectable in myocardium distal to the bridge. Among these subjects, 13 died suddenly and 6 during heavy exercise. These 13 tunneled segments were significantly deeper in the myocardium than the ones from the victims who did not die suddenly.

An increase in sympathetic drive during stress or exercise likely facilitates ischemia, because tachycardia leads to an increase of the systolic-diastolic time ratio at the expense of diastolic flow. Increased contractility during stress further aggravates systolic (and diastolic) compression. Endothelial dysfunction and coronary artery spasm may also contribute to constriction of the tunneled segment.

Clinical Presentation

Angina, myocardial ischemia, myocardial infarction, left ventricular dysfunction, myocardial stunning, paroxysmal AV blockade, as well as exercise-induced ventricular tachycardia and sudden cardiac death are accused sequelae of myocardial bridging. However, considering the prevalence of myocardial bridging, these complications are rare. Patients may present with atypical or angina-like chest pain with no consistent association between symptom severity and the length or depth of the tunneled segment or the degree of systolic compression.

Resting ECGs are frequently normal; stress testing may induce nonspecific signs of ischemia, conduction disturbances, or arrhythmias. Children with HOCM and myocardial bridges may have an increased QTc dispersion and a higher rate of monomorphic ventricular tachycardia on Holter ECG compared with subjects without myocardial bridges. Perfusion defects may be seen on myocardial scintigraphy but are not obligatory even in deep bridges with significant systolic compression or after vasoactive stimulation.

Coronary Angiography

The current gold standard for diagnosing myocardial bridges is coronary angiography with the typical “milking effect” and a “step down–step up” phenomenon induced by systolic compression of the tunneled segment (Figure 1). However, these signs provide little information on the functional impact at the myocardial level. In the presence of a proximal stenosis, myocardial bridging may only be identifiable after PTCA when higher intravascular pressures and reversed hypokinesis unmask myocardial bridging. In patients with thin bridges, the milking effect may be missed and new imaging techniques and provocation tests may be required to detect a bridge.

New Imaging Techniques

With the use of IVUS, intracoronary Doppler ultrasound (ICD), and intracoronary pressure devices, morphological and functional features of myocardial bridging can be visualized and quantified. The “half-moon phenomenon” is a characteristic IVUS observation, but its physiology and anatomy are not fully understood (Figure 5). It seems specific for the existence of myocardial bridging inasmuch as it is only found in tunneled segments but not in proximal or distal segments or in other arteries. In the presence of a half-moon phenomenon on IVUS, milking can be provoked by intracoronary provocation tests, even if the bridge was angiographically undetectable. IVUS-based frame-by-frame analysis of lumen area during the entire cardiac cycle can also be used to quantify the delay in relaxation after systolic compression. Further, IVUS pullback studies supported the absence of atherosclerosis within tunneled segments, although ~90% of patients showed plaque formation.
proximal to the bridge. When deep tunneled segments approach the right ventricular subendocardium, the trabeculated right chamber myocardium and the right ventricular cavity may be visible on IVUS.

In ICD studies, pullback of the Doppler-flow wire frequently reveals a characteristic flow pattern, the “fingertip phenomenon” or “spike-and-dome pattern.” This flow pattern had previously been described in experimental studies and consists of a sharp acceleration of flow in early diastole followed by immediate marked deceleration and a mid-diastolic pressure plateau. It can frequently be observed within and just proximal to the tunneled segment (Figure 6) and can be explained by an increased pressure gradient in early diastole as a result of reduced distal coronary resistance and delayed relaxation of the myocardial fibers with continuing lumen compression and the ensuing lumen gain.

Particularly in deep myocardial bridges, rapid diastolic forward flow may be preceded by end-systolic flow inversion as a result of a local increase in pressure above aortic driving pressures (Figure 6). These changes result in an increased diastolic/systolic flow ratio of almost 3.0, compared with values of 1.8 and 1.3 in normal controls and significant coronary artery stenosis, respectively. As in experimental studies, coronary flow reserves are frequently reduced to values below 3.0, which can be regarded as the lower limit of the norm in otherwise healthy individuals.

Myocardial bridging can also be visualized with the use of novel noninvasive imaging techniques such as electron beam tomography (EBT, Figure 7) and, potentially, multislice CT (MSCT), magnetic resonance tomography (MRT), or trans-thoracic Doppler echocardiography. Whether these tools have a sensitivity and specificity high enough to advocate its use for clinical or research purposes remains to be shown.

**Therapy**

In symptomatic patients, therapy may be initiated to improve quality of life, although hard evidence for a favorable effect on morbidity and mortality is missing. On the basis of the above mechanisms for ischemia, 3 treatment strategies have been explored: (1) negative inotropic and/or negative chronotropic agents, ie, β-blockers and calcium antagonists; (2) surgical myotomy and/or CABG; and (3) stenting of the tunneled segment.

Medication is considered first-line therapy. Intracoronary administration of a short-acting β-blocker attenuated vascular compression and early diastolic blood velocity. The systolic/diastolic flow ratio was normalized and anginal symptoms were alleviated. Volume loading may also reduce compression of the tunneled segment, whereas administration of nitroglyceride may aggravate compression and ischemia.

In subjects refractory to medication, surgical myotomy, first reported by Binet et al in 1975, abolishes clinical symptoms and is associated with reversal of local myocardial ischemia and an increase in coronary flow. Recently, minimally invasive myotomy was successfully performed. However, surgery should be limited to patients with severe angina and evidence for clinically relevant ischemia. In bridges that take a deep subendocardial course, the right ventricle may accidentally be opened during surgery, and a case of aneurysm at the site of myocardial cleavage has been reported. Thus, the risk associated with surgery should carefully be weighed against the usually uneventful long-term course even in patients with substantial systolic compression.

In 1995, Stables et al first reported coronary stenting as an interventional approach to severe myocardial bridging refractory to medication. Normalization of the pathological coronary flow profile, the reduced coronary flow reserve, and symptoms after stent deployment promised successful use of stents in these patients. In 11 patients with signs of ischemia but absence of other cardiac disorders, all patients had good angiographic outcome with a marked improvement in the angina score after 6 months and after 2 years of follow-up. However, at 7 weeks, 46% of patients required revascularization as a result of in-stent restenosis. To our knowledge, a total of 25 patients to date have been reported to have received coronary stents for myocardial bridging. In 50% of these cases, restenosis or major periprocedural complications were reported, including perforation of the artery. Despite a favorable long-term outcome in the above patients, too few subjects refractory to medication...
have thus far been treated with coronary stents and the rate of restenosis has been too high to generally recommend this approach in symptomatic patients.

**Prognosis**

Long-term prognosis in patients with isolated myocardial bridging is generally good. Five-year survival in 81 subjects aged 46 years was 97.5%, with neither of the 2 deaths related to the myocardial bridge. In another group of 61 patients aged 50 years with bridging of the LAD, 11-year survival was 98%, again with no deaths attributable to myocardial bridging. In these studies, none of the patients with otherwise normal coronary arteries sustained a myocardial infarction during follow-up. Among 21 patients monitored for 3.4 years, two patients with coexistent CAD experienced a myocardial infarction and underwent CABG. All other patients, including 7 with HOCM and 8 with normal coronaries remained event-free. In a recent 43-month follow-up study, one of the 35 patients died, 20% of patients continued to have CCS class I-II angina, and 63% of subjects required medication at the end of follow-up. In children with HOCM, myocardial bridging was suggested to be a highly significant independent predictor for 5-year mortality, but these findings were disputed by others.

**Clinical Relevance**

Myocardial bridging can occasionally generate clinically important complications, despite usually being a benign condition. A considerable number of studies and reports have enhanced our understanding of the pathophysiological mechanisms involved in these complications. Myocardial bridging must be considered especially in patients at low risk for coronary atherosclerosis but with angina-like chest pain or established myocardial ischemia. However, the low rate of clinical manifestation and the large variability of morphological, functional, and clinical presentations precludes sound recommendations for diagnosis and therapy on the basis of currently available reports, which are mostly on a limited number of patients. We agree with others that large multicenter clinical databases are required to identify criteria that justify the link between clinical signs or symptoms and the myocardial bridge as the primary culprit and which move beyond the current empirical approach to the clinical management of this frequent coronary anomaly.

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Key Words: myocardial bridging ▪ anatomy ▪ tunnelled artery ▪ arteries

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