Health Technology Assessment

STINGRAY™ CATHETER AND GUIDEWIRE FOR RECANALIZATION OF CORONARY CHRONIC TOTAL OCCLUSIONS: A RAPID EVIDENCE ASSESSMENT

March 2013

IHE INSTITUTE OF HEALTH ECONOMICS
ALBERTA CANADA

INSTITUTE OF HEALTH ECONOMICS

The Institute of Health Economics (IHE) is an independent, not-for-profit organization that performs research in health economics and synthesizes evidence in health technology assessment to assist health policy making and best medical practices.

IHE BOARD OF DIRECTORS

Health Technology Assessment

STINGRAY™ CATHETER AND GUIDEWIRE FOR RECANALIZATION OF CORONARY CHRONIC TOTAL OCCLUSIONS: A RAPID EVIDENCE ASSESSMENT

Prepared by: Ken Bond, BAH, BEd, MA
Liz Dennett, BSc, MLIS

Production of this document has been made possible by a financial contribution from Alberta Health Services. The views expressed herein do not necessarily represent the official policy of Alberta Health Services.

ACKNOWLEDGEMENTS

The authors of the report would like to thank Wendy McIndoo (IHE) for her support with editing and formatting the full report.

Corresponding Author

Please direct any inquiries about this report to Christa Harstall, charstall@ihe.ca.

Funding

This report was supported by a financial contribution from Alberta Health Services (AHS). The completed report was submitted to AHS in February 2013.

The views expressed herein do not necessarily represent the official policy of AHS.

Declared Competing Interest of Authors

Competing interest is considered to be financial interest or non-financial interest, either direct or indirect, that would affect the research contained in this report or create a situation in which a person's judgment could be unduly influenced by a secondary interest such as personal advancement.

The authors of this publication claim no competing interests.

Suggested Citation (ICMJE or Vancouver Style)

Institute of Health Economics. *Stingray™ catheter and guidewire for recanalization of coronary chronic total occlusions*. Edmonton AB: Institute of Health Economics. 2013.

Web Address

This publication is available for free download from the IHE website at: www.ihe.ca.

STINGRAY™ CATHETER AND GUIDEWIRE FOR RECANALIZATION OF CORONARY CHRONIC TOTAL OCCLUSIONS

Request

This response addressed a request for information from Alberta Health Services on behalf of the Royal Alexandra Hospital Cardiac Catheter Lab. The objective was to summarize the available evidence on the safety, efficacy, effectiveness, and potential cost-effectiveness on the use of the BridgePoint Medical System (consisting of the CrossBoss™ catheter, Stingray™ catheter, and Stingray™ guidewire) for the recanalization of refractory coronary chronic total occlusions (CTOs). The response also describes the relevant outcomes for studies of percutaneous coronary intervention (PCI) for coronary CTOs.

The specific aim of the response was to answer the following questions:

1. What is the clinical safety, efficacy, effectiveness, and cost-effectiveness of the BridgePoint System for recanalization for patients with coronary CTO eligible for PCI and refractory to conventional catheter and guidewire?
2. What potential outcomes might be relevant to collect if conducting a pilot study of the BridgePoint System for recanalization of coronary CTOs?

Background

"Recanalization" refers to the restoration of a lumen (canal) in a blood vessel by the formation of new channels following occlusion by a clot.[1] Significant progress in the last 15 years in the percutaneous (i.e., performed through the skin rather than through an open surgical procedure) management of coronary artery disease in patients with acute coronary syndromes and acute myocardial infarction (MI) has led to reducing the occurrence of restenosis, saved lives, reduced rates of MI, and enhanced quality of life compared with alternative treatments.[2] A subset of those patients with coronary artery disease also have chronic total occlusions (CTOs). CTOs are characterized by significant atherosclerotic vessel narrowing with lumen compromise that results in either complete interruption of antegrade blood flow as assessed by coronary angiography (true total occlusions) or with minimal contrast penetration through the lesion without distal vessel opacification (functional total occlusions).[2] The true prevalence of CTO in the general population is unknown because a proportion of patients with CTO who are either asymptomatic or minimally symptomatic do not undergo coronary angiography.[2] Notwithstanding this uncertainty, some authors estimate the prevalence of CTO to range from 14 to 35% depending on patient age and the artery involved.[2,3] Patients with coronary CTOs are usually referred to coronary artery bypass surgery or medical therapy when recanalization of coronary CTOs may be appropriate.[2] In addition, older patients are less likely to undergo percutaneous coronary CTO recanalization than are young people, despite the fact that older people present more frequently with coronary CTOs.[2] This disparity between frequency of CTO and PCI is thought to highlight the technical and procedural complexities of this lesion subtype and uncertainties regarding which patients might benefit from coronary CTO recanalization.[2,4] Not all patients may benefit from CTO recanalization and the strategies to select the best candidates for such treatment have yet to be defined.

For those in whom recanalization of a coronary CTO is considered appropriate, the rationale for recanalization is the relief of angina, the improvement of left ventricular function, and improved

survival and quality of life;[2,3] however, some researchers consider the evidence of potential benefit to be unclear.[5] Joyal et al.[6] conducted a systematic review and meta-analysis[6] summarizing the results of 13 observational studies examining clinical outcomes after successful versus failed CTO recanalization. The authors were unable to identify any studies comparing recanalization with medical management. The reviewed studies were published between 1979 and 2006 and included a total of 7288 patients with an average follow-up of 6 years (range 1 to 10). The studies varied in their use of angioplasty, bare metal stents, and drug eluting stents. The authors found that successful CTO recanalization appeared to reduce both all-cause and in-hospital mortality, need for subsequent coronary artery bypass graft (CABG), and residual/recurrent angina. There was no apparent impact on MI or major adverse cardiac event (MACE) rates. The study results are summarized in Table 1. Because the results of the review and meta-analysis were based on the results of observational studies, the findings were considered inconclusive. Nevertheless, the authors concluded that, despite the technical challenges of recanalization of CTOs and the higher risks to patients of serious complications and increased exposure to dye and radiation, long-term outcomes appear to be improved in the population of patients who undergo successful recanalization of a CTO.

Table 1: Potential benefits of successful versus failed recanalization of chronic total occlusions[6]

Outcome	Odds Ratio (95% CI)	Relative reduction in number of events (%)	Benefit of recanalization
All-cause mortality	0.56 (0.43–0.72	44	Yes
MI	0.74 (0.44–1.25)	---	No
MACE	0.81 (0.55–1.21)	---	No
CABG	0.22 (0.17–0.27)	78	Yes
Residual/recurrent angina	0.45 (0.30–0.67)	55	Yes
Complications	Non-significant result*	---	---
In-hospital mortality	0.34 (0.18–0.65)	66	Yes

CABG = coronary artery bypass graft, MACE = major adverse cardiac event, MI = myocardial infarction
*Actual result not reported

Clinical Problem: Coronary Chronic Total Occlusions

Despite recent advances in PCI devices and techniques that have allowed expert operators to tackle successfully complex cases of coronary CTOs, coronary CTOs remain the lesion subtype in which angioplasty is most likely to fail.[4] The clinical presentation of a CTO can be variable.[7] Within the context of PCI, successful recanalization of coronary CTOs is considered the most technically challenging lesion subset faced by interventional cardiologists, with procedural success rates much lower than those achieved in less than totally occluded coronary vessels or acutely occluded arteries.[2,5] As noted above, coronary CTOs are characterized clinically by significant atherosclerotic vessel narrowing with lumen compromise that results in either complete interruption of antegrade blood flow as assessed by coronary angiography (thrombolysis in myocardial infarction [TIMI] grade 0 flow) or with minimal contrast penetration through the lesion without distal vessel opacification (TIMI grade 1 flow).[2] Temporal criterion for coronary CTOs vary, but, in general, a total occlusion of duration >3 months is considered "chronic", though temporal criterion in studies can vary from >2 weeks to ≥3 months.[2,8] Success rates for treating CTOs using standard guidewires range from 55

to 90%.[4,8] The success rate of CTO PCI decreases with increases in parameters such as occlusion duration, length and amount of calcification, and number of previous attempts (Table 2).[8]

Coronary CTOs are complex lesions to treat percutaneously because it can be difficult to cross the site of occlusion with conventional guidewires and remain in an intraluminal position.[9] Indeed, the most common reason for failure when attempting recanalization of coronary CTOs is the inability to pass a wire through the proximal occlusion cap and to successfully pass a wire across the lesion into the true lumen of the distal vessel,[4] with up to 90% of aborted attempts being due to an inability to pass the wire.[7] Frequently, the wire ends up beneath the vessel lining, i.e., in the subintimal space.

Table 2: Patient and lesion characteristics affecting recanalization success[8]

Characteristic	Simple	Complex
Vessel diameter (mm)	≥3.0	<3.0
Occlusion length (mm)	≤20	>20
Calcium occluded segment	None to moderate	Severe
Tortuosity occluded segment	Minimal to moderate	Severe
Occlusion stump	Tapered	Blunt or absent
Distal vessel opacification	Good to excellent	Poor
Distal vessel disease	Absent or moderate	Severe
Tandem/multiple occlusions	No	Yes
Tortuosity proximal to occlusion	Minimal to moderate	Severe
Disease of the proximal segment	Absent or moderate	Severe
Expected guiding catheter support	Good	Poor
Ostial location	No	Yes
Previous attempts	No	Yes
Renal insufficiency	No	Yes
Expected patient tolerance*	Good	Poor

*Cardiac or respiratory failure, musculoskeletal or psychiatric disorders limiting the patient's ability to lie flat for prolonged periods.

Technology

The BridgePoint System (BridgePoint Medical, Minneapolis, MN) consists of three devices: a blunt-tipped catheter to pass the occlusion or to create a subintimal entry (CrossBoss™), a flat shaped balloon with side exit holes (Stingray™ catheter), and a small-diameter wire with an angled and sharpened tip (Stingray™ guidewire) to exit from these holes and reenter the true vessel lumen.

Regulatory status

The Stingray™ guidewire and balloon catheter and the Crossboss™ catheter were approved for marketing by Health Canada in 2010 and by the US Federal Drug Administration in 2009 and 2010

(Table 3). The devices were considered by the FDA to be substantially equivalent to devices currently marketed (510(k) approval).

Table 3: Health Canada and US FDA Approval

Device	Model no.	Health Canada	US FDA
Stingray™ guidewire	M-3004, M-3012	August 2010	February 2009
Crossboss™ catheter	M-2000	September 2010	April 2009
Stingray™ orienting balloon catheter	M-1000	September 2010	July 2010

Clinical use

The BridgePoint Medical System is the first, and currently only, set of tools specifically designed to facilitate the controlled crossing and subintimal re-entry into the true lumen distal to a CTO[3] and, as such, is designed to meet both the problem of the inability to pass a wire through the proximal occlusion cap and passing a wire across the lesion into the true lumen of the distal vessel.[4] While a CTO can be approached either antegrade or retrograde (in those patients in whom PCI by the antegrade approach has failed), the BridgePoint System has been developed for an antegrade approach.

The CrossBoss™ catheter is designed with a blunt proximal tip that can be rotated manually. The Stingray™ guidewire is intended to facilitate the placement of balloon dilatation catheters or other intravascular devices during percutaneous transluminal coronary angioplasty (PTCA) and percutaneous transluminal angioplasty (PTA).[3] Both the CrossBoss™ and Stingray™ catheters are intended for directing, steering, controlling, and supporting a guidewire in order to access discrete regions of the coronary and peripheral vasculature.

Limitations

The Stingray™ guidewires are not to be used in cerebral blood vessels.

Cost

The following costs for the Canadian market of the components of the Stingray system and CrossBoss catheter were provided by BridgePoint Medical in response to a request from IHE (Table 4).

Table 4: Canadian unit costs for the BridgePoint Medical System

Product	Unit Price (USD)
Stingray catheter	1150.00
CrossBoss catheter	875.00
Stingray guidewire (300 cm)	250.00
Stingray extension wire	75.00
Stingray guidewire (185 cm)	250.00

Guidelines

Appropriateness criteria for coronary revascularization[10] (the re-establishment of blood flow in a vessel via bypass, angioplasty, or stenting) were developed by a working group made up of representatives from the American College of Cardiology Foundation Appropriateness Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, and the American Society of Nuclear Cardiology. The indications considered were intended to represent the most common patient scenarios for which coronary revascularization is considered, a group of indications much larger than just those patients with coronary CTOs. Though clinical decision making in this area is incredibly complex (the authors estimated that 4,000 different scenarios would be needed to adequately account for the permutations of the relevant variables), scenarios were constructed using five variables: clinical presentation, severity of angina, extent of ischemia on noninvasive testing along with the presence or absence of other prognostic factors, extent of medical therapy, and extent of anatomic disease. Because clinical decision making often takes place without having the information provided by angiography, the panel rated the appropriateness of revascularization based upon the clinical features and coronary findings and not the appropriateness of diagnostic coronary angiography. The scenarios were rated based on the published literature on the risks and benefits of PCI and surgical coronary revascularization (though it was unclear if a systematic review was conducted to inform the ratings). When judging appropriateness, it was assumed that operators performing the procedures have appropriate clinical training and experience and have satisfactory outcomes as assessed by quality assurance monitoring. In addition, it was assumed that it was technically feasible to perform revascularization and that patients did not have comorbidities likely to increase substantially the procedural risk. Of the six scenarios including CTOs, three were considered definitely appropriate for revascularization:

1. CTO of one major epicardial coronary artery, without other coronary stenosis; intermediate-risk findings on noninvasive testing; receiving course of maximal anti-ischemic medical therapy, and Canadian Cardiovascular Society (CCS) angina class III or IV.
2. CTO of one major epicardial coronary artery, without other coronary stenosis; high-risk findings on noninvasive testing; receiving no or minimal anti-ischemic medical therapy, and CCS angina class III or IV.
3. CTO of one major epicardial coronary artery, without other coronary stenosis; high-risk findings on noninvasive testing; receiving course of maximal anti-ischemic medical therapy, and CCS angina class I–IV.

The authors of the criteria emphasize that the criteria are meant to provide a framework for discussions regarding revascularization between patients and physicians and for payers to use as the basis for the development of rational payment strategies to ensure that patients receive necessary, beneficial, and cost-effective cardiovascular care. Nevertheless, the use of the framework in clinical decision making requires considering the clinical characteristics of individual patients.

A consensus document[2,4] on percutaneous recanalization of chronically occluded coronary arteries was produced by an international panel of physicians. The two-part document describes definitions, prevalence, clinical presentation of CTOs, as well as technical approaches and clinical outcomes after PCI and describes novel devices for angioplasty of coronary CTOs. The consensus document was meant to be a statement of the "state of the art" of CTO angioplasty rather than a clinical

practice guideline on the management of coronary CTOs and does not aim to provide recommendations of the kind encapsulated in guidelines.

More recent systematic reviews of revascularization for CTO[6] have noted that revascularization of CTOs is considered appropriate when performed for highly symptomatic patients (class III-IV) with at least intermediate risk findings on noninvasive testing or less symptomatic patients. For patients in classes I to II, higher risk findings on noninvasive testing are required, as long as maximal anti-ischemic medical therapy is already provided. Nevertheless, appropriateness criteria do not specifically address complex percutaneous recanalization like that treated with the BridgePoint System. It should also be noted that the consensus document described above predates the trial and approval of the BridgePoint System. Hence, though the guidelines[4] discuss special devices for CTO recanalization, including lumen re-entry devices that were developed to facilitate guidewire re-entry into the true lumen after the creation of a dissection plane, the BridgePoint System, an apparently novel system, is not mentioned or discussed. Nonetheless, as reported below, the evidence on the potential benefits of the BridgePoint System are not the result of prospective, randomized trials comparing the tools with other contemporary angioplasty equipment and techniques, evidence the authors of the consensus document state is likely required before the widespread acceptance and utilization of such devices.[4]

Available Evidence

The following summary describes the results obtained from three primary research studies that assessed all or part of the BridgePoint Medical System for recanalization of coronary CTOs. Research still in progress on this topic is also described.

Quantity of research available

No health technology assessments, systematic reviews, meta-analyses, or randomized studies published during or later than 2005 were identified that assessed the efficacy and safety of the BridgePoint System. In addition, no studies were identified that examined cost-effectiveness of the BridgePoint System; however, aspects of the technology that may lead to potential cost savings are explored in the Discussion. The literature search and selection process is described in Appendices A and B. Four reports[3,11-13] that met the inclusion criteria provided information on three case series studies. The characteristics of the included studies are summarized in Table 5 below. The grey literature search identified the study registration information for one of the studies;[13] that information was used to supplement the published report of the study.[3]

Table 5: Summary of study characteristics

First author, publication year, country	Study design, Length of follow-up	Sample size Patient characteristics	Intervention	Clinical outcomes	Other outcomes
Tsuchikane 2012 Japan[11]	Single centre, single group, open label	n = 11	BridgePoint System	- MACE rate - Device success - Re-entry procedure success - Procedural success	- Procedural complications - Fluoroscopy time - Contrast volume
Werner 2011 Germany[12]	Multi-centre (n = 4), single group, open label	n = 42 Refractory CCTO as assessed by failure to cross CCTO with currently marketed guidewire	BridgePoint System (full system or CrossBoss™ only or Stingray™ only)	- Technical success - Procedural success† - MACE rate - Periprocedural MI - Coronary re-occlusion - Puncture site complications - Emergency CABG	- Mean procedure time - Mean fluoroscopy time
FASTS-CTO 2010 USA[3,13]	Multi-centre (n = 16), single group, open label	n = 147 Refractory CCTO as assessed by failure to cross CCTO with currently marketed guidewire	BridgePoint System	- Technical success - MACE rate	- Mean procedure time - Mean fluoroscopy time

CABG = coronary artery bypass graft, CCTO = coronary chronic total occlusion, MACE = major adverse cardiac event, MI = myocardial infarction

†Procedural success was defined as successful stent deployment and reestablishment of TIMI (thrombolysis in MI) flow

Summary of Critical Appraisal

The quality of the conduct of each of the three case series studies[11-13] was assessed(Appendix C). The three studies were prospectively designed, described explicitly the eligibility criteria for the participants, and included participants at a similar point in their disease. One of the main outcomes, MACE rate, was a composite adverse event. It was unclear if participants were selected consecutively, how long the study follow-up period was, and if any participants were lost to follow-up. Of the two published studies, one[11] declared the authors' competing interests (consultation for

several large medical device manufacturers), but not the source of funding for the study. The other study[12] declared no potential financial conflicts of interest; however, the declaration failed to indicate that one of the study authors is the BridgePoint Medical company founder and chief operating officer.

Summary of findings

Two published studies[11,12] were found, one that reported the results of a small single centre study conducted in Japan and one that reported results from a multi-centre case series study conducted in Germany. A third, larger multi-centre case series study[13] was conducted in the United States and coordinated by BridgePoint Medical as part of the FDA approval process. The study was registered prior to its conduct[13] and the study results were reported by Werner[3] in an article describing the BridgePoint System.

Results from Tsuchikane et al.[11]

Tsuchikane et al.[11] conducted a prospective, single centre, single group study with 11 patients (10 male, 1 female; mean age 60 years ± 6) to evaluate the BridgePoint System for a simplified antegrade approach to facilitate guidewire entry into the true lumen of a CTO from the adjacent subintimal space. Patients were eligible for the study if they if they had a previous coronary angiogram demonstrating CTO in one of their native coronary arteries. No patient was excluded because of adverse angiographic features such as severe calcification, tortuosity, lack of a visible entry point, or excessive lesion length; however, patient selection depended on the availability of the device, so patients were not enrolled consecutively. The BridgePoint System was also used as a rescue alternative after unsuccessful antegrade wiring with a conventional wire. In these cases the CrossBoss™ was not used to advance the Stingray™ balloon catheter. In cases of unsuccessful antegrade revascularization using this system, a retrograde approach was used to achieve procedural success. The main outcomes were MACE rate (no time specified and including all death, emergent bypass surgery, repeated revascularization, Q-wave or non-Q wave MI, any vascular complications, and contrast induced nephropathy), device success (successful revascularization), re-entry procedure success (successful puncture using Stingray™ catheter and guidewire), and procedural success (achievement of final TIMI flow grade 3 without residual stenosis >50%), and procedural complications. Secondary outcomes were fluoroscopy time and contrast volume.

The BridgePoint System was used in 11 CTO cases: primary use for eight cases and rescue use in three. There were no MACE between the time of the procedure and discharge the next day. Overall device success rate was 8/11 (72.7%); 7/8 (87.5%) in the primary group and 1/3 (33.3%) in the rescue group. Re-entry success was achieved in 3/8 (37.5%) of primary cases. In rescue cases, re-entry success was achieved in 1/3 cases. Re-entry procedure success rate was 4/5 (80%; in three cases the occlusion was crossed using the CrossBoss™ and did not require re-entry) in the primary group and 1/3 (33.3%) in the rescue use group. Mean fluoroscopy time was for the primary group was 41.3 minutes (±28.2) and 88.7 min (±35.2) for the rescue group. Procedural success was achieved for all patients (11/11); however, in three cases a retrograde approach had to be used. Procedural complications were not reported. Contrast volume was 181 mL (±115) in the primary use group and 307 mL (±61) in the rescue group. The study results are summarized in Table 6.

Table 6: Results from Tsuchikane et al.[11]

Outcome	Result (no. participants)	Result (%)
Device success[†]	Overall: 8/11 Primary group: 7/8 Rescue group: 1/3	Overall: 72.7 Primary group: 87.5 Rescue group: 33.3
Re-entry procedure success[‡]	Overall: 5/8** Primary group: 4/5 Rescue group: 1/3	Overall: 62.5 Primary group: 80.0 Rescue group: 33.3
Procedural success[§]	Overall: 11/11*	Overall: 100
Procedural complications	NR	NR
MACE	Overall: 0/11	Overall: 0
Fluoroscopy time	Primary group: 41.3 min (± 28.2) Rescue group: 88.7 min (± 35.2)	
Contrast volume	Primary group: 181 mL (± 115) Rescue group: 307 mL (± 61)	

NR = not reported

*Three cases of unsuccessful re-entry procedure were successful using a retrograde approach.

[†]Defined as successful revascularization

[‡]Defined as successful puncture using Stingray™ catheter and guidewire

[§]Defined as achievement of final TIMI flow grade 3 without residual stenosis >50%

**In three cases the occlusion was crossed using the CrossBoss™ and did not require re-entry

Results from Werner et al.[12]

Werner et al.[12] conducted a prospective, four-centre, single group study with 42 participants to evaluate the ability of the CrossBoss™ and Stingray™ catheters and Stingray™ guidewire to facilitate safe and effective intra-luminal placement of a guidewire beyond CTO without significant increase in major complications as compared with conventional guidewire/support catheter. Study participants were eligible for recanalization due to chest pain or persistent occlusion after a prior MI and had coronary artery CTOs refractory to conventional guidewire and catheter equipment and technique. The four operators involved in the study were considered to have a high level of experience with PCI of CTOs. Refractoriness (i.e., resistance to treatment) was defined as the inability to successfully cross the CTO in 20 minutes or less of procedure time or where best effort in recanalization resulted in the guidewire entering the subintimal space. The complexity of the CTOs was considered high (mean lesion length = 37mm) with half the CTOs located in the right coronary artery. The main outcomes were technical success, which was defined as the BridgePoint Medical System facilitating the placement of a guidewire in the true lumen distal to the CTO, and 30-day MACE rate. Secondary outcomes were death, periprocedural MI, puncture site complications, emergency coronary artery bypass graft (CABG), procedure time, and procedural fluoroscopy time.

Technical success was achieved in 28/42 cases (67%) with procedural success following in all 28/42 (67%) of these cases. Reasons for technical failure included failure to cross the CTO cap (n = 5), inability to advance the Stingray™ balloon to a proper position (n = 2), inability to direct the Stingray™ wire into the true distal lumen (n = 2), inability to advance the Stingray™ balloon upon

re-entry after wire advancement (n=3), and re-entry puncture failure due to loss of distal contrast filling (n = 2). Technical success appeared higher in those cases in which the CrossBoss™ and Stingray™ were used in sequence (71%) compared with cases in which the Stingray™ was used on its own after subintimal passage with conventional wire (50%). The mean procedure time was 110 min ±60 and mean fluoroscopy time 41.4 min ±22.1. Adverse events occurred in 2/42 (4.7%) of participants, both of whom had periprocedural non-ST evaluation MI after successful recanalization. Both participants were asymptomatic with a peak enzyme rise within 24 hours of the procedure and were discharged without further complications. There were no perforations with either the CrossBoss™ catheter or Stingray™ balloon and Stingray™ re-entry wire. The study results are summarized in Table 7. The authors concluded that the CrossBoss™ catheter helped to facilitate passage of the proximal cap and may help less experienced operators achieve CTO crossing in patients with certain angiographic exclusion criteria. The authors also state that the Stingray™ balloon catheter has potential for guided re-entry but optimum use requires proper and continued training and an experienced operator.

Table 7: Results from Werner et al.[12]

Outcome	Result (no. participants)	Result (%)
Technical success*	28/42	67
Full system (n = 14)	10/14	71
CrossBoss only (n = 18)	13/18	72
Stingray only (n = 10)	5/10	50
Procedural success†	28/42	67
MACE rate	2/42	4.7
Death	0	0
Periprocedural MI	2/42	4.7
STEMI	0	0
NSTEMI	2/42	4.7
Coronary reocclusion	0	0
Puncture site complications	0	0
Emergency CABG	0	0
Mean procedure time (SD)	110 min (± 60)	---
Mean procedural fluoroscopy time (SD)	41.4 min (± 22.1)	---

CABG = coronary artery bypass graft, MACE = major adverse cardiac event, MI = myocardial infarction, NSTEMI = non-ST evaluation, STEMI = ST evaluation

*Defined as the BridgePoint Medical System facilitating the placement of a guidewire in the true lumen distal to the CTO

†Defined as successful deployment and reestablishment of TIMI (thrombolysis in myocardial infarction) 3 flow

Results from FASTS-CTO[3,13]

The FAST-CTO study was a prospective, 16-centre, single group study with 147 participants conducted to evaluate the ability of the CrossBoss™ and Stingray™ catheters and Stingray™ guidewire to facilitate safe and effective intra-luminal placement of a guidewire beyond coronary CTO without significant increase in major complications as compared with conventional

guidewires/support catheters. Refractoriness was defined as a previously failed attempt to cross the occlusion or a concurrent attempt to cross the occlusion within 10–15 minutes of fluoroscopy time with guidewires of the operators' choice or entry into the subintimal space during this 10–15 minutes of fluoroscopy time. The main outcome was technical success, which was defined as the BridgePoint Medical System facilitating the placement of a guidewire in the true lumen distal to the CTO. Secondary outcomes were 30-day MACE rate (a composite outcome comprising cardiac death, lesion-related acute myocardial infarction, emergency bypass surgery involving the treated segment), procedure time, and fluoroscopy time. Technical success was achieved in 114/147 (77%) of participants with 7 (4.8%) participants experiencing a MACE. The mean procedure time was 105 minutes and the mean fluoroscopy time 44 min. The main results are summarized in Table 8. Werner[3] concluded that the CrossBoss™ catheter used upfront after conventional wire failure reduced procedure time.

Table 8: Results from FASTS-CTO[3,13]*

Outcome	Result (no. participants)	Result (%)
Technical success[†]	114/147	77
MACE rate	7/147	4.8
Mean procedure time	105 min (median: 96 min)	---
Mean fluoroscopy time	44 min (median: 41 min)	---

MACE = major adverse cardiac event

*Results from this study have been presented only at medical conferences and were reported by Werner.[3]

[†]Defined as the BridgePoint Medical System facilitating the placement of a guidewire in the true lumen distal to the CTO

Additional Studies

Werner[3] reports that the results from earlier small studies conducted in Europe evaluating the BridgePoint System in refractory CTOs after conventional wire attempts have been reported only at medical conferences. Device success rates from these European studies are reported to be 67%. The literature search and selection also identified 2 single case reports[14,15] describing the use of the BridgePoint System for refractory CTOs.

Limitations

As the BridgePoint System is currently the only device available with which to attempt recanalization for refractory CTOs, the only comparisons that can be made are to other treatment modalities. No such comparisons were identified. Hence, the efficacy and safety of the device and procedure must be assessed without either direct or indirect comparative data. Though the study sizes may appear small, the highly select patient population represents a small fraction of those patients who may be eligible for PCI of coronary CTO. Werner et al.[12] reported that the 42 participants in that study constituted only 15% of all patients with CTO treated during the 1-year study period. It should also be highlighted that the assessment of the potential of a new device for coronary CTOs is difficult to assess because a major factor for success is the operator's experience and skill,[3,12] and there is a learning curve associated with gaining this skill.[3,12]

Outcomes to Evaluate PCI of Coronary CTO

As well as requesting evidence of safety and efficacy, AHS requested a list of outcomes that might be relevant to a pilot study of the BridgePoint System. In addition to those short-term outcomes reported above in Joyal et al.[4] and Werner et al.,[12] Stone et al.[2,4] reported short- and long-term outcomes developed by a consensus panel that may be potentially useful for a pilot study. The outcomes reported by these authors are presented below (Table 9)

Table 9: Potential outcomes for study of the BridgePoint Medical System

Effectiveness	
Short-term	Technical success (full system, CrossBoss only, Stingray only)*
	Procedural success*
	Functional recanalization
	Anatomical recanalization
	In-hospital mortality
	Total procedure time*
	Total procedural fluoroscopy time*
Long-term	Need for surgical revascularization
	All-cause mortality
	Need for CABG
	Freedom from angina
	Residual/recurrent angina
Safety	30-day MACE (including cardiac death)*
	12-month cardiac death or MI
	1-year event-free survival
	Periprocedural MI (STEMI, NSTEMI)*
	Coronary reocclusion*
	Emergency CABG*
	Puncture site complications*

CABG = coronary artery bypass graft, MACE = major adverse cardiac event, MI = myocardial infarction, NSTEMI = non-ST evaluation, STEMI = ST evaluation
*Outcomes reported by Werner et al.[12]

Expert Opinion

The experts contacted who were working within Alberta were unable to provide information regarding the prevalence or incidence of chronic CTOs in Alberta, the devices currently being used by interventional cardiologists, and the current use of the BridgePoint Medical system within Alberta (especially the training required to gain facility with the device and the number of procedures per year that ought to be done to maintain a high level of skill with the system).

Discussion

The results of this rapid review indicate that the procedural success rate of PCI of coronary CTOs may be improved by the use of the BridgePoint System. However, the reader should bear in mind

that these observations are the results of three, relatively small, non-comparative studies. Nevertheless, the nature of the procedure and seriousness of the main clinical outcomes (MACE and procedural success) are such that confidence in the estimate of benefits may not require studies with large numbers. Studies of the BridgePoint System have not formally compared the Stingray™ and Crossboss™ devices with conventional wire and catheter using other techniques in totally occluded vessels. Hence, clinical researchers[4] believe that a randomized trial would provide useful evidence with respect to the relative effectiveness and safety of this and other similar devices.[4]

Overall technical success rates in Werner[3] and FASTS-CTO studies were 67% and 77%, respectively and the difference in results may be largely a result of the lower success rate of the "Stingray-only" group in the Werner study, which achieved a success rate of 50%. When only those in whom the full BridgePoint System had been employed were considered, the technical success rate was 72%. MACE rates in the two studies were also similar at 4.7% and 4.8%, respectively, as were procedure and fluoroscopy times.

One weakness of the studies reviewed was the limited amount of evidence regarding patient important and long-term outcomes listed in Table 9. The majority of evidence on potential benefits are on technical outcomes and safety, the main indicator of which is the 30-day MACE rate. As the benefits for recanalization are focused on reducing angina and mortality and improving ventricular function and quality of life, having better evidence on these outcomes is desirable.

Daniels et al.[16] reported a study of 101 consecutive patients who received PCI with either the CrossBoss™ catheter and Stingray™ re-entry system or wire only approach. Compared with the wire-only approach, the antegrade success rate for those in whom the BridgePoint System was used was significantly higher (86% vs. 64%, p = 0.022) and required lower conversion rate to a retrograde approach (12% vs. 32%, p = 0.02).[16] However, this study was reported only in abstract form and was excluded for this reason because of the limited information abstracts provide on patient and other characteristics of importance for assessing the effectiveness and safety of the technology and generalizing to actual practice.

Extensive contrast use and fluoroscopy times can result in contrast nephropathy and dermatologic x-ray toxicity, conditions that can lead to death, as can arrhythmias, hemorrhagic complications, and air embolism, all of which are more common with prolonged complex procedures.[4] Hence, any reductions in contrast use and fluoroscopy and procedure times are likely desirable and should be seen as proxy measures for potential reductions in these sequelae.

Given the technical skills and knowledge required for successful PCI, it is likely that surgeon experience and training influences the successful use of the BridgePoint System. Indeed, the outcome data of at least two of the studies reviewed here, and likely the third as well, were the result of PCI in the hands of very experienced interventional cardiologists working in high-volume centres. Other review authors[3,17]have noted the difficulty of assessing potentially new devices for CTO because of the inherent learning curve with a new device and the importance of operator experience and skill for achieving success. The question remains regarding what amount of training and continuing experience with the BridgePoint Medical System is needed to ensure a high likelihood of procedural and patient success.

Though Canadian studies may have helped to provide important information regarding the use of this device in the Alberta context, only one potentially relevant Canadian study[18] was identified. This study was reported only in abstract form (and was excluded for that reason); however, it also

provided little evidence to address the question as the BridgePoint System was used in only 3 of 108 patients and indications were not confined to coronary occlusions.

Performance

Case selection remains one of the most important predictors of PCI success.[7] The success rate of CTO recanalization varies widely (Ge[7] reports a range of 18% to 87%) depending on the nature of the occlusion (complete versus functional), its duration (the concern of this review was chronic occlusions, that is, those >3 month duration), occlusion length, whether or not there is a side branch at the point of occlusion, the presence of a tapered stump, the presence of bridging collaterals, as well as other factors such as the extent of calcification, vessel disease, and the presence of unstable angina.[7]

Additionally, experts in PCI intervention[4] have stated that "there is general confusion regarding the accepted indications for PCI of chronic occlusions, the optimal technical approach, and the ultimate impact of revascularization on patient outcomes. The procedural complexity of angioplasty in CTOs and the lack of familiarity with new equipment and technique innovations specific to CTO intervention often prompt half-hearted prematurely aborted attempts at PCI, ensuring high failure rates and physician and patient frustration." This confusion and lack of familiarity may mean that more widespread use of tools specific for the recanalization of chronic CTOs may not achieve the same performance as in studies. Hence, adequate training and quality assurance mechanisms are likely required to ensure the potential benefits of these new tools are realized in practice.

Expanding Indications for Use

Published case reports have indicated the potential benefit of expanding the indications for this device.[19,20] In January, 2012, BridgePoint Medical, Inc. completed a 10-centre, single-group study to examine the safety and effectiveness of the BridgePoint System for lower extremity CTOs.[21] The study enrolled 105 patients. The primary outcomes for the trial are:

- Incidence of patients with a major adverse events (death, major unplanned amputation, perforation requiring intervention, or target lesion revascularization due to complication) within 30 days
- Incidence of intraprocedural technical success

At the time of this update, the study results had not yet been published. The success of this study may lead to the approval of the devices for this additional indication.

Economic Impact

As noted above, the BridgePoint System has the potential to reduce fluoroscopy times, the volume of contrast medium required, and overall procedure times. These savings will act to reduce the overall cost of the procedure because of reduced OR time and reduced staffing time. In addition, costs linked to adverse events related to the use of contrast medium may be reduced. Though a formal cost-effectiveness analysis would be required to estimate the potential cost savings that may be realized within the Alberta context, we were unable to obtain an estimate of the current prevalence of this procedure within the province, information that is crucial to estimating the potential cost-savings.

Limitations

This rapid review of the research literature has several methodological limitations. The literature review was confined to reports of primary and secondary research studies that were published in the English language and were publicly available. Only full text articles were included for data extraction because abstracts provide insufficient details to allow a detailed, accurate, and appropriate comparison of the study results.

The fact that only one reviewer performed study selection and data extraction, though less than ideal, was not considered a serious weakness because of specificity of the technology and the relatively small amount of literature available on this topic. Relatedly, the present review only summarizes the recommendations from reports of relevant clinical practice guidelines and consensus documents and does not appraise their scientific foundations.

Conclusions

The BridgePoint Medical System has been developed specifically to address two main challenges in performing PCI for coronary CTOs: passing a wire though the occlusion cap and re-entering the true lumen of the occluded vessel. The evidence on the clinical effectiveness and safety of the BridgePoint System for recanalization of coronary CTOs is limited to that provided by three small non-comparative studies, the evidence from the largest of which was considered sufficient for licensing purposes in both Canada and the United States. In addition, there is at least one known study evaluating the use of these devices for additional indications and which may lead to expanded use of the devices.

References

1. McDonough JT Jr, ed. *Stedman's concise medical dicationary illustrated*, 2nd edition. "Recanalization." Baltimore: Williams & Wilkins; 1994. p.870.
2. Stone GW, Kandzari DE, Mehran R, Colombo A, Schwartz RS, Bailey S, et al. Percutaneous recanalization of chronically occluded coronary arteries: A consensus document: Part I. *Circulation* 2005;112:2364-72.
3. Werner GS. The BridgePoint devices to facilitate recanalization of chronic total coronary occlusions through controlled subintimal reentry. *Expert Review of Medical Devices* 2011;8(1):23-9.
4. Stone GW, Kandzari DE, Mehran R, Colombo A, Schwartz RS, Bailey S, et al. Percutaneous recanalization of chronically occluded coronary arteries: A consensus document: Part II. *Circulation* 2005;112:2530-7.
5. de LA, Bonello L, Roy P, Lemesle G, Steinberg DH, Xue Z, et al. Comparison of safety, efficacy, and outcome of successful versus unsuccessful percutaneous coronary intervention in "true" chronic total occlusions. *American Journal of Cardiology* 2008;102(9):1175-81.
6. Joyal D, Afilalo J, Rinfret S. Effectiveness of recanalization of chronic total occlusions: a systematic review and meta-analysis. *American Heart Journal* 2010;160(1):179-87.
7. Ge JB. Current status of percutaneous coronary intervention of chronic total occlusions. *Journal of Zhejiang University - SCIENCE B (Biomedicine & Biotechnology)* 2012;13(8):589-602.
8. Kim HY. Percutaneous recanalization of coronary chronic total occlusions: current devices and specialized wire crossing techniques. *Sunhwangi* 2010;40(5):209-15.
9. Al-Ameri H, Clavijo L, Matthews RV, Kloner RA, Shavelle DM. Devices to treat peripheral chronic total occlusions. *Journal of Interventional Cardiology* 2012;25(4):395-403. Available: http://www.scopus.com/inward/record.url?eid=2-s2.0-84864595963&partnerID=40&md5=c28e708f80bfac2b244a8c850d638c20.
10. Patel MR, Dehmer GJ, Hirshfeld JW, Smith PK, Spertus JA. ACCF/SCAI/STS/AATS/AHA/ASNC 2009 appropriateness criteria for coronary revascularization. *Journal of the American College of Cardiology* 2009;53:530-53.
11. Tsuchikane E, Kimura M, Suzuki T, Habara M, Kurita T, Tanaka N, et al. New re-entry device for revascularization of chronic coronary total occlusions: Preliminary single Japanese center experience. *Journal of Invasive Cardiology* 2012;24(8):396-400.
12. Werner GS, Schofer J, Sievert H, Kugler C, Reifart NJ. Multicentre experience with the BridgePoint devices to facilitate recanalisation of chronic total coronary occlusions through controlled subintimal re-entry. *Eurointervention* 2011;7(2):192-200.
13. *Facilitated antegrade steering technique in chronic total occlusions (FAST-CTOs).* 2010. NCT00886899. Available: http://clinical.trials.gov/ct2/show/NCT00886899?term=stingray&rank=2 (accessed 2011 Sep 15).

14. Brilakis ES, Lombardi WB, Banerjee S. Use of the Stingray guidewire and the Venture catheter for crossing flush coronary chronic total occlusions due to in-stent restenosis. *Catheterization & Cardiovascular Interventions* 2010;76(3):391-4.

15. Jessup DB, Lombardi W. Re-canalization of peripheral chronic total occlusions using the BridgePoint Stingray Re-entry Device. *Journal of Interventional Cardiology* 2011;[e-article ahead of print]:1-5.

16. Daniels D, Tremmel J, Yeung A, Lombardi W. Cto pci using device based antegrade dissection and re-entry: Improving success for all comers. *Journal of the American College of Cardiology Conference: 61th Annual Scientific Session of the American College of Cardiology and i2 Summit: Innovation in Intervention, ACC 12 Chicago, IL United States Conference Start: 20120324 Conference End: 2012032* 2012;(var.pagings):E105.

17. Alaswad K. Toolbox and Inventory Requirements for Chronic Total Occlusion Percutaneous Coronary Interventions. *Interventional Cardiology Clinics* 2012;1(3):281-97.

18. Rinfret S, Joyal D, Mansour S, Nguyen C, Leung R, Hui W, et al. A simplified 4-wire strategy to cross chronic total occlusions; early Canadian experience. *Canadian Journal of Cardiology* 2011;27:S182 (abstract 330).

19. Galbraith EM, Del RM, Niazi K. Use of the stingray re-entry system in two complex cases of occluded superficial femoral arteries. *Case Reports in Vascular Medicine Print* 2011;2011:976312, 2011.

20. Luna M, Banerjee S, Brilakis ES. Use of the CrossBoss catheter for crossing superficial femoral artery chronic total occlusions. *Cardiovascular Revascularization Medicine* 2012;13(1):58-61.

21. *Peripheral facilitated antegrade steering technique in chronic total occlusions (PFAST-CTOs)*. 2011. Available: http://clinicaltrials.gov/ct2/show/NCT01246505?term=bridgepoint&rank=3 (accessed 2011 Sep 15).

Appendix A: Methods

A literature search was designed and conducted by the IHE Research Librarian in the following major electronic bibliographic databases: MEDLINE, The Cochrane Library, CRD Database.

Table A.1: Literature search summary

Database	Edition or date searched	Search Terms[††]
Core Databases		
EBM reviews (Ovid Interface) includes Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (2005 - September 2012) ACP Journal Club (1991 to August 2012) DARE, HTA Database, and NHS EED (all 3rd Quarter 2012)	Oct 3, 2012	1. (stingray or bridgepoint or crossboss).tw. 2. occlu*.mp. 3. (catheter* or microcatheter* or guidewire or Re-entry or recanali*).tw. 4. 1 and (2 or 3) (0 results)
MEDLINE (include in process articles) (OVID interface)	Oct 3-2012 1946-Oct 3, 2012	1. (stingray or bridgepoint or crossboss).tw. 2. occlu*.mp. 3. (catheter* or microcatheter* or guidewire or Re-entry or recanali*).tw. 4. 1 and (2 or 3) (11 results)
Embase (Ovid Interface)	Oct 3, 2012 1996-2012 Week 39	1. (stingray or bridgepoint or crossboss).tw. 2. occlu*.mp. 3. (catheter* or microcatheter* or guidewire or Re-entry or recanali*).tw. 4. 1 and (2 or 3) (15 results)
Web of Science (ISI Platform)	Oct 3, 2012	TS=(stingray or bridgepoint or crossboss) TS=(occlu* or catheter* or microcatheter* or guidewire or Re-entry or recanali*) #1 AND #2 (9 results)
Scopus	Oct 3, 2012	(TITLE-ABS-KEY(stingray OR bridgepoint OR crossboss) AND TITLE-ABS-KEY(occlu* OR catheter* OR microcatheter* OR guidewire OR re-entry OR recanali*)) (20 results)

HTA Agencies		
INESSS (http://www.inesss.qc.ca/)	Oct 3, 2012	Occlusion; catheter; guidewire; recanalization; recanalisation; crossboss; stingray; bridgepoint 1 potentially relevant result
CADTH (http://www.cadth.ca/en/products)	Oct 3, 2012	Occlusion and (catheter or guidewire); recanalization; recanalisation; crossboss; stingray; bridgepoint; percutaneous 2 relevant results
Medical Advisory Secretariat http://www.hqontario.ca/en/mas/mas_ohtas_mn.html	Oct 3, 2012	Occlusion; catheter; guidewire; recanalization; recanalization; percutaneous; stingray; crossboss; bridgepoint 0 relevant results
ICES (http://www.ices.on.ca/)	Oct 3, 2012	Occlusion; catheter; guidewire; recanalization; recanalization; percutaneous; stingray; crossboss; bridgepoint
Clinical Trials		
Clinicaltrials.gov	Oct 3, 2012	Stingray OR crossboss OR bridgepoint
Search Engines		
Google	Oct 3, 2012	chronic total occlusion stingray OR crossboss OR bridgepoint –pubmed Reviewed first 50 results

Methods

Literature search

MEDLINE, Cochrane Library and CRD electronic bibliographic databases were searched for abstracts describing HTAs, systematic reviews, and reports of randomized and non-randomized studies. The search was limited to documents published in English from 2005 onward. A search of the grey literature was also conducted. The search was originally conducted September 2011 and updated October 2012.

Literature Selection

A single reviewer assessed the relevance of the retrieved citations and the full text of potentially relevant reports using the following selection criteria (Table A2).

Table A.2: Study selection criteria

Population	Patients with coronary CTO or in-stent restenosis requiring recanalization
Intervention	CrossBoss™ catheter, Stingray™ balloon catheter, and Stingray™ guidewire
Comparator	Conventional or other guidewire/support catheter technology
Outcomes	Any outcome relevant to patient safety, efficacy, effectiveness, cost-effectiveness
Study Designs	Health technology assessment (HTA), systematic review or meta-analysis, randomized controlled trial, non-randomized study (excluding reports of single cases)

Studies were excluded if they did not meet any one of the above inclusion criteria.

Assessment of methodological quality

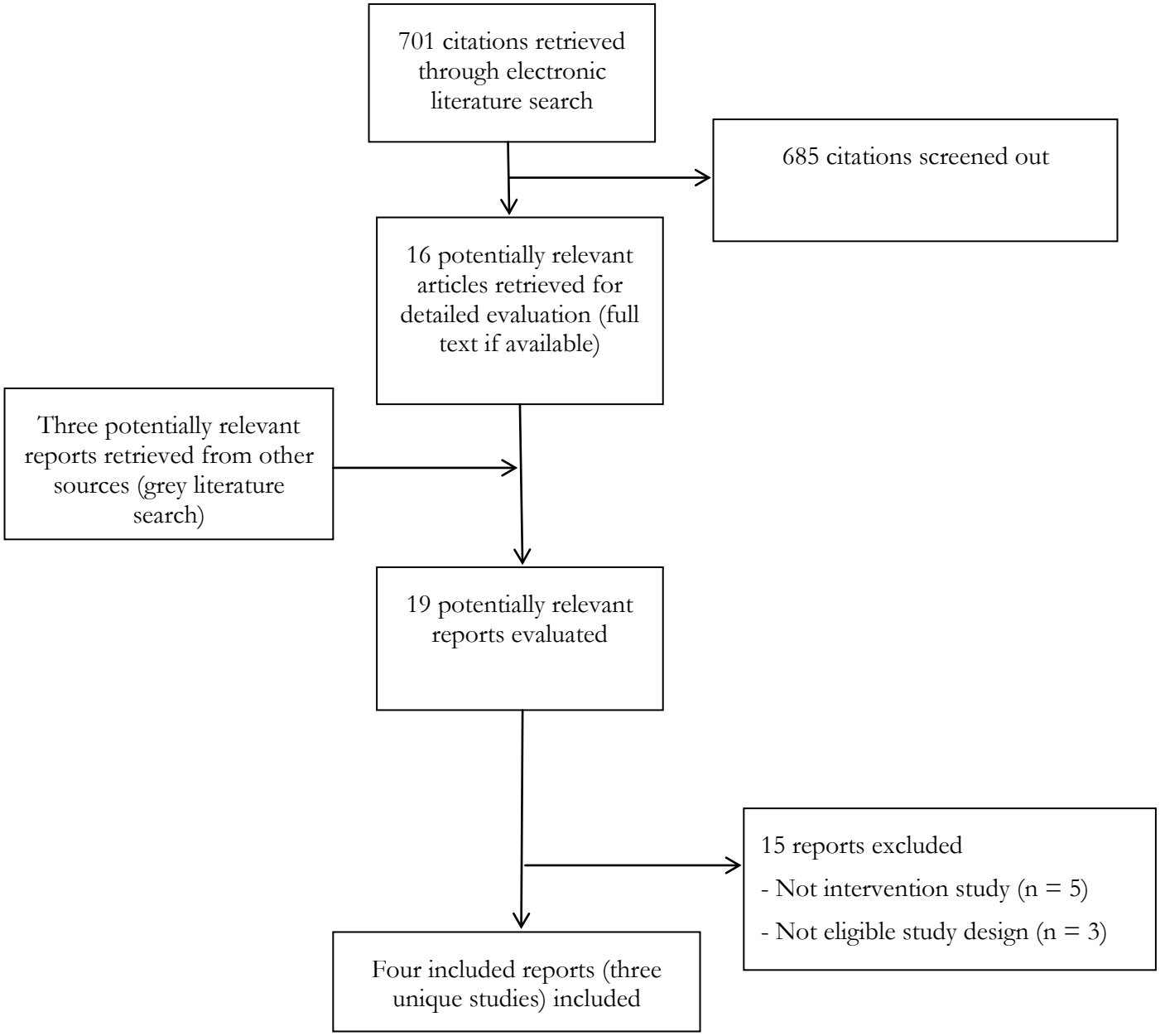
The methodological quality of the studies was assessed using a tool developed by the IHE for case series studies and used in previous HTA reports. A single reviewer appraised the studies according to the following nine items:

1. Prospective or retrospectively conduct
2. Consecutive recruitment of study participants
3. Explicit eligibility criteria
4. Study participants enrolled at similar timepoint in disease
5. Main outcomes assessed blind/independent to intervention status
6. Length of follow-up reported
7. Losses to follow-up reported
8. Adverse events reported
9. Competing interests and source of financial support reported

Data extraction and summary

A single reviewer extracted data and summarized the available information. Based on the abstracts that met the predefined selection criteria, a tabular and narrative summary of characteristics and quality of evidence was developed. References for included studies are provided. The list of excluded studies along with reason for exclusion is available upon request.

Appendix B: Selection of Included Studies on the BridgePoint System



Appendix C: Critical Appraisal of Included Studies

No.	Criterion	FASTS-CTO 2010[13]	Tsuchikane et al. 2012[11]	Werner et al. 2011[12]
Recruitment				
1	Was the study conducted prospectively?	Yes	Yes	Yes
2	Were participants recruited consecutively?	Unclear	No	Unclear
Population				
3	Are the eligibility criteria (inclusion and exclusion criteria) to entry the study explicit and appropriate?	Yes	Yes	Yes
4	Did participants enter the study at a similar point in the disease?	Yes	No†	Yes
Outcome				
5	Were the main outcomes assessed blind/independent to intervention status?	No	No	No
6	Was the length of follow-up reported?	No	No	No
7	Was the lost to follow-up reported?	No	No	No
8	Are adverse events reported?	Yes	Yes	Yes
Competing interest and source of support				
9	Are both competing interest and source of support for the study reported?	No	No	Yes*

*The conflict of interest statement failed to indicate that one of the authors is the BridgePoint company founder and chief operating officer. The potential conflicts of interest of the other authors is unknown.

†Study included patient receiving PCI for primary revascularization and those receiving rescue PCI.

Contributors Statements

Ken Bond wrote the review protocol, conducted the literature selection, quality assessment, and data extraction, summarized and interpreted the study results and wrote the report.

Liz Dennett designed and conducted the literature search.

Christa Harstall assisted with the writing of the protocol, revised the manuscript for critical content, and approved the final version for publication.

The review summarizes the current evidence on the safety, efficacy, effectiveness, and potential cost-effectiveness on the use of the BridgePoint Medical System (consisting of the CrossBoss™ catheter, Stingray™ catheter, and Stingray™ guidewire) for the recanalization of refractory coronary chronic total occlusions (CTOs). The report also describes the relevant outcomes for studies of percutaneous coronary intervention (PCI) for coronary CTOs.

Institute of Health Economics
1200 – 10405 Jasper Avenue
Edmonton AB Canada T5J 3N4
Tel. 780.448.4881 Fax. 780.448.0018
info@ihe.ca

www.ihe.ca

ISBN 978-1-926929-06-4 (on-line)