Ontario
Health Quality Ontario

Mitral Valve Clip for Treatment of Mitral Regurgitation: OHTAC Recommendation

HEALTH QUALITY ONTARIO

ONTARIO HEALTH TECHNOLOGY ADVISORY COMMITTEE RECOMMENDATION

- OHTAC recommends that the mitral valve clip procedure be funded in centres of excellence identified by the Cardiac Care Network (CCN), and that all such centres enroll all patients receiving the mitral valve clip procedure in a CCN-supported registry

BACKGROUND

Caused by valvular dysfunction, mitral regurgitation is the abnormal backflow of blood into the left atrium during cardiac systole that is normally prevented by the bicuspid mitral valve. (1) Mitral regurgitation may be acute or chronic. Acute mitral regurgitation is a medical and surgical emergency and is invariably treated surgically. (2) For chronic mitral regurgitation, surgical repair or replacement of the mitral valve is the current standard of care when patients become symptomatic with severe mitral regurgitation, dilated ventricles, new-onset atrial fibrillation, or pulmonary hypertension. (2)

Chronic mitral regurgitation is etiologically heterogeneous. The two most common categories are *degenerative* (myxomatous/fibroelastic deficiency causing flail leaflets or floppy valve leading to ineffective coaptation) and *functional*. (3) In functional mitral regurgitation, the mitral apparatus is structurally normal, but its geometry is distorted. This may occur with left ventricular dilatation, ventricular remodelling, or dyssynchronous contraction of the left and right ventricles as observed post–myocardial infarction or in cardiomyopathy. (4) Surgical treatment of functional mitral regurgitation is less well established. (5)

Surgical correction of mitral regurgitation may employ valve repair or replacement (with or without preservation of the mitral apparatus). Surgical mitral valve repair is the treatment of choice in most cases because it preserves the mitral apparatus and competence, and does not require the lifelong anticoagulation needed if the valve were replaced by a prosthetic device. (6) Similar rates of reoperation (a postsurgical complication) have been observed following both valve repair and replacement, that is, about 20% over 19 years. (7)

Despite the availability of the valvular repair option, the risk of undertaking the surgery may be too high or prohibitive; the Society of Thoracic Surgeons states that the risk of mortality is ≥ 8%. (8) In general this translates into a subgroup of symptomatic patients who are elderly, are frail, have several comorbidities, and have a history of previous cardiac procedures and/or hemodynamic instability. Many of the 500,000 North American patients with chronic mitral regurgitation may be poor candidates for mitral valve surgery. (9)

As alternatives to surgery, various mitral valve repair procedures that employ a percutaneous approach are under investigation, such as edge-to-edge leaflet repair and indirect and direct annuloplasties. (3)

Approved in Canada, the United States, and Europe, the mitral valve clip is one percutaneous mitral valve repair option. It was first used in humans in 2003. (10) The mitral valve clip system consists of the clip device, a delivery system, and a catheter guide through which the delivery system is introduced trans-septally into the left atrium toward the mitral valve through a femorovenous approach. Mitral valve clips have been implanted in more than 10,000 patients. (5) The clip device is conceptually based upon the commonly employed surgical edge-to-edge Alfieri technique of suturing the opposing leaflets in the middle, thereby creating two orifices (with reduced regurgitation area) for blood flow across the mitral opening. (11, 12)

The Evidence Development and Standards branch at Health Quality Ontario commissioned the Ottawa Hospital Research Institute Methods Centre—Evidence-Based Practice Centre (OMC-EPC) to perform an evidence-based analysis to answer the research questions below.

REVIEW OF THE EVIDENCE

Research Questions

- For symptomatic patients at high or prohibitive surgical risk, what are the comparative effectiveness, harms, and cost-effectiveness of percutaneous mitral valve repair using a mitral valve clip?
- What are the important population effect modifiers?

Main Findings

- Evidence was generally inadequate to explore subgroup effect modification, including differences in estimates of effectiveness and harms by mitral regurgitation etiology
- The majority of the direct comparative evidence compares percutaneous mitral valve clip repair with surgery in patients not particularly at prohibitive surgical risk
- In low-surgical-risk populations with chronic mitral regurgitation, important limitations in design, power, and generalizability of evidence preclude definitive conclusions about the relative benefit or harms of the mitral valve clip procedure when compared with surgery
- Within the intervention arm, however, the mitral valve clip did meaningfully improve mitral regurgitation, New York Heart Association (NYHA) functional class, and quality of life (by 4 or 5 points on a scale of 100) from baseline values
- Very low quality of evidence indicates that percutaneous mitral valve clip repair may provide a survival advantage, at least during the first 1 to 2 years, especially in medically managed chronic functional mitral regurgitation
- Across the studies, when compared with surgery, mitral valve clip repair was not found to be definitively harmful. However, 20 to 25% of patients who received a mitral valve clip subsequently underwent valve surgery because of clip failure
- As such, there is an unmet need for the use of this emerging technology in patients with chronic mitral regurgitation who are at prohibitive surgical risk who are either in poor functional status or at risk of progression toward it, despite drug therapy. The true advantage may be greater in patients with functional mitral regurgitation, but our confidence for this hypothesis is very low. However, the cost-effectiveness of mitral valve clips in patients at prohibitive risk for surgery could not be established

- Future studies should investigate the pragmatic clinical scenario of treating patients with mitral regurgitation who are at prohibitive surgical risk, versus conservative management, while controlling for important confounding biases and adjusting for participant attrition

For a fuller discussion and the evidence related to these recommendations, please see the related report.

OHTAC DELIBERATIONS

Health Quality Ontario has developed a decision-making framework to help guide deliberation and support the development of OHTAC recommendations regarding the uptake, diffusion, distribution, or removal of health interventions in Ontario. Table 1 provides a summary of the decision determinants for this recommendation.

Decision Determinants

Table 1: Decision Determinants for Mitral Valve Clip Use for Mitral Regurgitation

Decision Criteria	Subcriteria	Decision Determinants Considerations
Overall clinical benefit How likely is the health technology/intervention to result in high, moderate, or low overall benefit?	**Effectiveness** How effective is the health technology/intervention likely to be (taking into account any variability)?	In low-risk surgical candidates, the comparative effectiveness and harms of mitral valve clips are uncertain, but substantial improvement from baseline in NYHA functional class, quality of life, and severity of regurgitation were seen with mitral valve clips. Very low quality of evidence indicates that percutaneous mitral valve clip repair may provide survival advantage at least over the first 1–2 years especially in medically managed chronic functional MR.
	Safety How safe is the health technology/intervention likely to be?	When compared with surgery, mitral valve clip repair was not found to be definitively harmful. However, 20–25% of mitral valve clip recipients may have to subsequently undergo valve surgery because of clip failure.
	Burden of illness What is the likely size of the burden of illness pertaining to this health technology/intervention?	About 9% of the elderly have MR. About 50% of these patients may have severe MR. Up to 49% of elderly patients with severe MR may be at prohibitive risk for surgery.
	Need How large is the need for this health technology/intervention?	There is an unmet need for the use of this emerging technology in patients with chronic MR who are at prohibitive surgical risk who are either in poor functional status or at risk of progression toward it, despite drug therapy.

Decision Criteria	Subcriteria	Decision Determinants Considerations
Consistency with expected societal and ethical values[a] How likely is adoption of the health technology/intervention to be congruent with societal and ethical values?	**Societal values** How likely is the adoption of the health technology/intervention to be congruent with expected societal values?	Unclear.
	Ethical values How likely is the adoption of the health technology/intervention to be congruent with expected ethical values?	The ethical conundrum is this: can we deny this nonsurgical treatment to a vulnerable symptomatic and functionally compromised population at prohibitive risk for conventional surgical treatment in whom we expect potential benefit but have uncertainty about serious harms, based on a very low quality of evidence?
Value for money How efficient is the health technology likely to be?	**Economic evaluation** How efficient is the health technology/intervention likely to be?	The efficiency of mitral valve clips cannot currently be established due to the uncertainty regarding the comparative outcomes of a mitral valve clip versus surgery or medical management. Additional comparative evidence is required.
Feasibility of adoption into health system How feasible is it to adopt the health technology/intervention into the Ontario health care system?	**Economic feasibility** How economically feasible is the health technology/intervention?	The economic feasibility of mitral valve clips is unclear due to uncertainty regarding the efficiency of the technology relative to current standards of care. If recommended, the technology should be used only in cardiac catheterization laboratories with multidisciplinary teams (an interventional cardiologist, a geriatric cardiologist, cardiac surgeons, imaging specialists, electrophysiologists, perfusionists, etc.).
	Organizational feasibility How organizationally feasible is it to implement the health technology/intervention?	

Abbreviations: MR, mitral regurgitation; NYHA, New York Heart Association.

[a]The anticipated or assumed common ethical and societal values held in regard to the target condition, target population, and/or treatment options. Unless there is evidence from scientific sources to corroborate the true nature of the ethical and societal values, the expected values are considered.

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DISCLAIMER

The analysis may not have captured every relevant publication and relevant scientific findings may have been reported since the development of this recommendation. This report may be superseded by an updated publication on the same topic.

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