

Cor-Knot for tying suture knots in valve surgery

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is Cor-Knot. It is used for securing sutures in open and minimally invasive valve surgery.
- The **innovative aspects** according to the company are that the device provides a quicker, more consistent and secure knot than hand-tied knots.
- The intended **place in therapy** would be as an alternative to hand-tied knots in people having open and minimally invasive valve surgery, or an alternative to endoscopic knot pushers, which are used in minimally invasive valve surgery.
- The **main points from the evidence** summarised in this briefing are from 5 studies, including a systematic review of 2 randomised controlled trials and 6 retrospective cohort studies, and 4 observational studies. The studies involve a total of 1,715 adult patients in secondary care. They show that Cor-Knot may reduce aortic cross-clamp time and cardiopulmonary bypass time when used in valve surgery compared with standard care.

- **Key uncertainties** around the evidence or technology are that there is limited high-quality evidence, with only 2 randomised controlled trials and limited evidence of follow up of patients to assess the long-term efficacy of Cor-Knot.
- **Safety issues** raised for the technology include that some patients develop post-operative valve regurgitation after Cor-Knot damaged the valve leaflets. The company acknowledges a very low rate of leaflet perforation (0.0021%) and that appropriate fastener orientation prevents leaflet damage. The company states reported adverse events are low (0.00015%) and claims events are primarily related to surgical technique. There is limited evidence of follow up of patients to assess the long-term safety of Cor-Knot.
- The **cost** of Cor-Knot is £650 to £750 per patient (not including VAT), depending on the number of knots tied. The **resource impact** would be greater than standard care. However, this could be offset if there are greater benefits, such as reduced adverse events, reduced length of stay or time saving during procedures. Evidence to support these claims is limited.

The technology

Cor-Knot (LSI Solutions) is a single-use device to replace hand-tied surgical knots in valve surgery, including open and minimally invasive mitral valve repair, and aortic valve replacement. The Cor-Knot device consists of a handle, lever and shaft.

There are 2 sizes of device: Cor-Knot MIS (31 cm length, 5 mm diameter shaft) and Cor-Knot Mini (17 cm length, 4 mm diameter shaft). The Cor-Knot Mini device also contains a rotational knob with an indicator fin which is intended to help the user with suture orientation.

Add-ons include the Cor-Knot quick load unit, which is used to load a single, sterile titanium fastener (Cor-Knot fastener) into the Cor-Knot device. Squeezing the applicator lever secures the suture (by crimping the fastener) and trims the suture tails at the same time. Cor-Knot devices must be used with the Cor-Knot fastener. The company states that Cor-Knot is designed to be used with the company's specified suture (LSI 2-0 polyester sutures) but other 2-0 polyester sutures can be used.

Innovations

The innovative aspects according to the company are that the device provides a quicker, more consistent and secure knot than hand-tied knots. The company claims that Cor-Knot reduces cardiopulmonary bypass time, reduces aortic cross-clamp time and reduces the risk of paravalvular leak.

Current care pathway

Aortic valve replacement with an artificial prosthesis (biological or mechanical) is the conventional treatment for people with severe aortic valve dysfunction. Valves may be placed using open heart surgery or transcatheter aortic valve implantation (TAVI).

If someone is referred for surgery, a cardiac surgeon determines whether open or minimally invasive surgery is more appropriate for them. Currently cardiac surgeons use hand-tied knots in minimally invasive and open valve surgery procedures. Endoscopic knot pushers can be used in minimally invasive valve surgery.

Other options for aortic valve replacement are:

- Sutureless aortic valve replacement for aortic stenosis, which involves removing the narrowed aortic valve and replacing it with an artificial valve that keeps itself in place. The procedure may be quicker than conventional surgical aortic valve replacement, because the valve does not need to be sewn in, which reduces cardiopulmonary and aortic cross-clamp times.
- TAVI for aortic stenosis is a less invasive alternative to open cardiac surgery for treating aortic stenosis, avoiding the need for sternotomy and cardiopulmonary bypass.
- Valve-in-valve TAVI (for treating failed bioprosthetic aortic valves originally placed by either open heart surgery or TAVI) is a less invasive alternative treatment that avoids the need for cardiopulmonary bypass.

Degenerative mitral regurgitation is treated by surgery to repair or replace the mitral valve. The mitral valve can be repaired by thoracoscopically assisted mitral valve surgery. People who cannot have open surgery can have percutaneous mitral valve leaflet repair for mitral regurgitation.

The following NICE interventional procedures guidance has been identified as relevant to this care pathway:

- [Valve-in-valve TAVI for aortic bioprosthetic valve dysfunction](#)
- [Percutaneous mitral valve leaflet repair for mitral regurgitation](#)
- [Sutureless aortic valve replacement for aortic stenosis](#)
- [Transcatheter aortic valve implantation for aortic stenosis](#)
- [Thoracoscopically assisted mitral valve surgery](#).

Population, setting and intended user

Cor-Knot is for use in people who need valve surgery, including conventional and minimally invasive mitral valve repair, and aortic valve replacement. If surgery is appropriate, a cardiac surgeon determines whether it should be open or minimally invasive.

Cor-Knot is likely to be used in secondary care by cardiac surgeons. The company states that it could be used in around 2,500 heart valve procedures each year in the UK. Training is provided by the company and included in the cost of the device. It involves teaching the theatre team to unpack, handle and load the device, and then practise in a dry laboratory demonstration. Education and training is ongoing. The company also provides clinical specialists to support cases and training.

Costs

The cost of a single heart valve replacement or repair procedure ranges from £8,025 to £14,813 ([HRG codes ED24A-C and ED25A-C](#)) for elective procedures.

Technology costs

The cost per patient of Cor-Knot varies according to the number of knots tied. A mitral valve procedure using 15 fasteners costs £787.50. An aortic procedure using 12 fasteners costs £632.00. The list prices for Cor-Knot are:

- standard Cor-Knot Device £315.00 for a pack of 2 (maximum 12 sutures each)

- Cor-Knot Mini device £254.00 for a pack of 2
- Cor-Knot Quick Load Fastener £378.00
- Cor-Knot Quick Load Fastener £2,266.00 for 6 pouches.

Costs of standard care

Non-absorbable sterile 2-0 sutures cost from £1.07 to £1.93 per suture ([NHS Drug Tariff](#), accessed December 2019). A patient who has valve surgery would typically need 9 to 18 sutures, depending on the surgery. A reusable knot pusher costs between £500 and £2,000, according to the company. Additional instruments would also be needed, such as laparoscopic scissors.

Resource consequences

Cor-Knot has been launched in the UK, and according to the company is currently being used in 32 trusts.

The resource impact is in addition to standard care, but this could be offset if using Cor-Knot has benefits over hand knotting, such as reducing adverse events, length of hospital stay or procedure time. But there is limited evidence to support this.

Regulatory information

Cor-Knot Device and Cor-Knot Quick Load Unit are CE-marked class III medical devices.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Cor-Knot is intended for use in people having valve surgery. Older people are more likely to need surgery for degenerative aortic valve disease. They may also have comorbidities that can contribute to operative mortality so need a careful preoperative assessment (in line with [NHS England's service specifications for cardiac surgery in adults](#)). Age is a

protected characteristic under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Five studies are summarised in this briefing, involving a total of 1,715 patients.

The studies summarised are 1 systematic review (which assesses 2 randomised controlled trials and 6 retrospective cohort studies), and 4 observational studies.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

Many studies evaluate Cor-Knot in valve surgery. The most relevant are included in this briefing and include outcomes such as cardiopulmonary bypass time and aortic cross-clamp time. These are relevant because of the company claims that Cor-Knot may reduce these times. The systematic review by [Salmasi et al. 2019](#) includes 8 studies, of which 2 are randomised controlled trials. The studies that were not randomised or controlled are generally of a low methodological quality.

Some safety issues have been identified with Cor-Knot. [Sagheer et al. 2019](#) reported a metallic embolus in the brain of a patient 7 months after valve surgery with Cor-Knot. The embolus is thought to have originated from the metallic valve or the Cor-Knot fastener. [Garrett Jr 2017](#) report a delayed metallic embolisation 5 years after robotic mitral valve repair using Cor-Knot, which caused a stroke in the patient. The company said that after it discussed the case with Dr Garrett, they concluded that the metallic embolisation was not caused by Cor-Knot. The author highlights the need for long-term surveillance after using Cor-Knot.

Navas-Blanco et al. 2018 reported a full thickness injury to the left coronary sinus during an aortic valve replacement after using Cor-Knot. The company says this was a result of unusually thin tissue and operator error. Baciewicz Jr 2018, Biefer et al. 2018, Brescia et al. 2017 and Balan et al. 2017 reported patients developing post-operative valve regurgitation after Cor-Knot damaged the valve leaflets. The company acknowledges that 9 in 438,000 cases (0.0021%) result in leaflet perforation. The authors highlight the need to orient the Cor-Knot fastener away from the prosthesis and for meticulous technique. Biefer et al. 2018 also suggested that a rigid mitral ring may be a better valve prosthesis because they have not had any episodes of perforation since using this. The company acknowledges that 11 titanium fasteners out of more than 7,188,000 sold have been involved in reported adverse events, with a complaint rate of 0.00015%. The company says the events are primarily related to surgical technique and that appropriate fastener orientation prevents leaflet damage.

More high-quality controlled trials in the NHS are needed to compare patient outcomes with Cor-Knot with hand-tied knots and endoscopic knot pushers. These studies should include long-term follow up to assess the longer-term efficacy and safety of Cor-Knot.

Salmasi et al. (2019)

Study size, design and location

A systematic review and meta-analysis of 8 studies (6 retrospective cohort studies, 2 randomised controlled trials) comparing operative efficacies between Cor-Knot and manual knot tying in patients undergoing aortic valve replacement (AVR) or mitral valve repair. Location: UK.

Intervention and comparator(s)

Intervention: Cor-Knot.

Comparator: manual knot tying.

Key outcomes

Four studies looked at AVR (Loberman et al. 2018, Beute et al. 2018, Lee et al. 2018 and Plestis et al. 2018). In these studies aortic cross-clamp time was significantly shorter with Cor-Knot than with manual tied knots. The weighted mean difference (WMD) was 86.62

(95% confidence interval [CI] 15.9 to 157.4; $p=0.016$). Cardiopulmonary bypass time was shorter in 2 studies: median 86 minutes (interquartile range [IQR] 40) for Cor-Knot compared with 113.5 minutes (IQR 42), $p=0.02$; and mean 104 minutes (± 22.5 minutes) for Cor-Knot compared with 118.3 minutes (± 30.1 minutes), $p<0.001$. However, there was no difference in another study, which reported a mean of 100.1 minutes (± 21.3 minutes) using Cor-Knot compared with 107.3 minutes (± 20.4 minutes), $p=0.1$. The fourth study did not record cardiopulmonary bypass time. A meta-analysis of the 4 studies showed no significant difference for 30-day mortality between Cor-Knot and hand tying (odds ratio 1.73; 95% CI 0.50 to 6.02; $p=0.678$). Using Cor-Knot did not increase the risk of permanent pacemaker implantation, paravalvular leak, or 30-day mortality. Five studies reported length of intensive care stay, 4 reported no difference between the 2 groups. One study showed significantly reduced time in hospital with Cor-Knot: a median of 6 days (range 4 days to 17 days) compared with 7 days (range 4 days to 79 days), $p=0.002$.

Four studies looked at mitral valve repair ([Grapow et al. 2015](#), [Etiwy et al. 2018](#), [Sabik et al. 2018](#) and [Perin et al. 2019](#)). Meta-analysis of these studies showed significantly reduced cardiopulmonary bypass time in the Cor-Knot group compared with the manual knot tying group (WMD: 110.0; 95% CI 12.3 to 207.7; $p=0.027$). There was also significantly shorter aortic cross-clamp time in the Cor-Knot group (WMD: 79.0; 95% CI 10.4 to 147.5; $p=0.024$). There were no differences in length of intensive care or hospital stay.

Strengths and limitations

The systematic review with meta-analysis is high-quality evidence. Statistical analysis of the relevant outcomes helps to objectively assess efficacy of Cor-Knot compared with standard care.

The authors excluded publications if cardiopulmonary bypass time or aortic cross-clamp time were not reported, limiting the number of studies reviewed. The mitral valve intervention papers included minimal access studies and combined tricuspid repair studies, which may have affected operative times and outcomes. Only 2 randomised controlled trials were included. The remaining 6 were retrospective cohort studies, which are lower quality evidence.

Morgant et al. (2019)

Study size, design and location

A single-centre prospective study involving 221 patients undergoing isolated AVR surgery with stented prosthesis between September 2009 to June 2018. Location: France.

Intervention and comparator(s)

Intervention: Cor-Knot (n=63).

Comparator: Hand-tied knots (n=158).

Key outcomes

Compared with the hand-tied knot group, the Cor-Knot group had shorter aortic cross-clamp time (74 minutes [\pm 13.8 minutes] compared with 90.4 minutes [\pm 23.7 minutes], $p < 0.0001$) and cardiopulmonary bypass times (100.8 minutes [\pm 20.6 minutes] compared with 117.6 minutes [\pm 33.1 minutes], $p < 0.0001$). The differences in 30-day mortality (1.2% and 0%, $p = 0.37$) and stroke and transient ischaemic attack rates (2.5% and 1.6%, $p = 0.67$) between the 2 groups were not statistically significant.

Strengths and limitations

Statistical analyses were done using a propensity score with 1:1 matching for automatically tied and hand-tied knots, helping comparability of outcomes between the 2 groups. Large sample size helps to improve reliability. The study was not done in the UK and so is not generalisable to the NHS.

Nifong et al. (2013)

Study size, design and location

A single-centre retrospective observational study involving 336 patients receiving Cor-Knot or robot-assisted mitral valve repair between May 2000 and December 2012. Location: USA.

Intervention and comparator(s)

Intervention: Cor-Knot (n=48).

Comparator: robotic suture tying (n=288).

Key outcomes

The mean time to place and secure sutures was significantly shorter for Cor-Knot compared with robotic knot tying (107.4 seconds [\pm 50.4 seconds] compared with 151.8 seconds [\pm 71.4 seconds], $p < 0.02$). Three other outcome times were also significantly shorter for Cor-Knot than for robotic tying:

- annuloplasty band placement (26.9 minutes [\pm 7.4 minutes] and 36.6 minutes [\pm 10.2 minutes], $p < 0.02$)
- cardiopulmonary bypass (144.9 minutes [\pm 30.1 minutes] and 160.3 minutes [\pm 40.1 minutes], $p < 0.02$)
- aortic cross clamp (94.7 minutes [\pm 31.1 minutes] compared with 123.0 minutes [\pm 33.3 minutes], $p < 0.02$).

Strengths and limitations

The study is presented as a conference abstract, which is low-quality evidence, and with limited reporting of outcomes. It is not in the UK and so not generalisable to the NHS. The study period (from 2000 to 2012) is relatively old and therefore potentially less useful. There were fewer patients in the Cor-Knot group than in the robotic suture tying group, with no information about the groups' baseline characteristics. This limits comparability of outcomes between the 2 groups.

Wang et al. (2017)

Study size, design and location

A retrospective observational study involving patients undergoing minimally invasive aortic valve replacement (MIAVR) during 2002 and 2015. Location: USA.

Intervention and comparator(s)

Intervention: MIAVR with adjuncts (Cor-Knot, coronary sinus catheter; n=78).

Comparators: MIAVR without adjuncts (n=78), AVR through a median sternotomy (n=78).

Key outcomes

There was no difference in preoperative preparation time between the MIAVR with adjuncts group and the MIAVR without adjuncts group (83.1 minutes compared with 81.1 minutes, $p=0.56$, CI -4.7 to 8.6). MIAVR with adjuncts had shorter cross-clamp time (70.5 minutes compared with 108.1 minutes, $p<0.0001$, CI 31.1 to 44.0) and shorter cardiopulmonary bypass time (101.1 minutes compared with 166.1 minutes, $p<0.0001$, CI 54.0 to 76.1) compared with the without adjuncts group. Compared with patients who had AVR via sternotomy, MIAVR with adjuncts also had shorter cross-clamp time (70.5 minutes compared with 84.4 minutes, $p<0.0001$, CI 8.2 to 19.6) and cardiopulmonary bypass time (101.1 minutes compared with 127.7 minutes, $p<0.0001$, CI 19.3 to 33.9).

Strengths and limitations

Patients who had MIAVR with adjuncts were propensity matched against those who had MIAVR without adjuncts and AVR through median sternotomy for comorbidities such as age, gender and ejection fraction. This made baseline characteristics similar, allowing comparability. The procedures were performed by 12 surgeons, which helps to increase the reliability of the results. The type of prosthesis used varied between the groups, which may have affected outcomes. The MIAVR with adjuncts group included Cor-Knot and coronary sinus catheter, so it's not possible to attribute outcomes solely to Cor-Knot.

Liang et al. (2019)

Study size, design and location

A single-centre retrospective cohort study involving 114 patients who had MIAVR for isolated aortic valve disease between January 2011 and August 2018. Location: USA.

Intervention and comparator(s)

Intervention: Cor-Knot, single-shot del nido cardioplegia, and rapid deployment valves.

Comparator: no facilitating technology.

Key outcomes

After Cor-Knot was introduced, compared with no facilitating technology, aortic cross-clamp time reduced from a median of 96 minutes (IQR 84 to 103) to 84 minutes (IQR 73 to 90); $p < 0.001$. Cardiopulmonary bypass time reduced from a median of 157 minutes (IQR 134 to 182) to 129 minutes (IQR 113 to 144); $p < 0.001$.

Strengths and limitations

This is a single-centre study, and 98% of the procedures were done by the same surgeon, which limits the reliability of the results. Cor-Knot was introduced in 2012. Only the outcomes for aortic cross-clamp time and cardiopulmonary bypass time were reported for Cor-Knot. Other outcomes were reported after 2 other interventions were introduced, which makes results difficult to interpret or attribute to an individual intervention. Only 2 of the 114 people in the study were women.

Sustainability

The company has not submitted any sustainability claims.

Recent and ongoing studies

[Multi-center register for the use of the Cor-Knot automated knotting system in heart valve surgery \(RECORVA\)](#). ClinicalTrials.gov identifier: NCT03681834. Status: not yet recruiting. Indication: vascular surgery. Last update posted September 24, 2018. France. Devices: Cor-Knot.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Five experts had used this technology. All have significant experience of it and continue to use it. All said that the technology is widely used in the NHS for minimally invasive surgery.

Level of innovation

All experts said that the technology is a novel concept and the only product available to perform this function. Two said the technology is a complete replacement for hand-tied knots. None of the experts was aware of any competing products.

Potential patient impact

All experts agreed that the technology would be beneficial for minimally invasive surgery. Four believed using the technology reduces cross-clamp and bypass time or would shorten procedure time in general. One said the technology could improve the speed of knotting. Four experts said that the technology results in a securer, more accurate knot.

Potential system impact

All experts acknowledged the benefit of this technology in helping minimally invasive surgery. All said that the technology costs more than standard care. Two experts believed the increased cost of the technology could be offset by reduced patient length of stay. One also believed the technology would reduce the amount of blood product needed for surgery. Two experts said that the technology would help in complex surgery. One felt shorter procedure time would be a benefit for people who are older. All experts believed training is needed but that training was simple. Three felt the technology could change the care pathway for minimally invasive surgery. One expert felt the effect of the technology should first be investigated in more clinical trials. Four experts referenced the case reports of aortic valve leaflet perforation as a safety concern, but 2 said that they happen because of inaccurate orientation of the device. One expert has completed a recent audit of more than 150 cases in their trust and reported no adverse events.

General comments

Three experts said the technology works well, or they have found it helpful, particularly in difficult cases. Three said the cost is likely to be a barrier to adoption. Three experts felt NICE guidance would help. One queried whether NICE guidance would help because the technology is already widely used. One expert believed guidance would be useful for surgeons planning a non-sternotomy approach to cardiac valve surgery.

Expert commentators

The following clinicians contributed to this briefing:

- Mr Ishtiaq Ahmed, consultant cardiac surgeon, Royal Sussex County Hospital. No interests to declare.
- Mr Enoch Akowuah, consultant cardiothoracic surgeon, South Tees Hospital NHS Foundation Trust. No interests to declare.
- Mr Venkatachalam Chandrasekaran, St George's University Hospital NHS Foundation Trust. No interests to declare.
- Mr Narain Moorjani, consultant cardiothoracic surgeon, Royal Papworth Hospital. No interests to declare.
- Mr Joseph Zacharias, consultant cardiothoracic surgeon, Blackpool Victoria Hospital. Mr Zacharias received funding to recruit a 12-month fixed-term minimal access fellow to complete an audit, and has visited LSI solutions facilities for training.

Development of this briefing

This briefing was developed by NICE. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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