BMC Surgery

STUDY PROTOCOL

Open Access

Assessment of a novel unidirectional mid-term absorbable barbed suture versus a competitor barbed suture for vaginal cuff closure after gynaecology surgery, study protocol of a randomized controlled trial - BARHYSTER

Petra Baumann[1*], Lourdes Hinojosa Sánchez[2], Núria Grané Garcia[2], Larisa Sologiuc[3,4] and Amadeus Hornemann[3,4]

Abstract

Background Total laparoscopic hysterectomy (TLH) is nowadays the standard to treat benign and malignant disease occurring in the uterus, but the number of robotic-assisted surgeries is increasing worldwide. To facilitate the handling of sutures in a bi- and tri-dimensional plane, a new type of suture material has been developed, named barbed sutures, which are in use in different indications. In comparison to conventional suture materials, the barbs anchor the suture in the tissue, provide tissue approximation and prevent slippage without the need for knot tying. Several meta-analyses and systematic reviews have shown that they are safe and efficient. The current study investigates the clinical outcome of a novel unidirectional mid-term absorbable barbed suture which differs in its configuration from other barbed sutures. The collected data will be prospectively compared to the results of a competitor's unidirectional mid-term absorbable barbed suture and retrospectively to the findings reported for conventional sutures after hysterectomy in the literature.

Methods An international, randomised, multicentric, single-blinded design was chosen. A total of 132 patients will be included receiving randomly either the novel unidirectional barbed suture versus the competitor unidirectional barbed suture in a 3:1 ratio. Both suture materials will be applied to close the vaginal cuff after laparoscopic hysterectomy and the time for suturing is the primary endpoint. As secondary objectives, the following parameters will be collected and compared in both suture groups: intraoperative handling of the suture material, quality of life using the Female Sexual Function Index (FSFI), patient satisfaction, pain, and complications occurring in the short-term and long-term follow-up. For each patient, the study lasts 6 months after surgery.

Discussion This study will assess the clinical performance of a novel unidirectional mid-term absorbable barbed suture material for the first time in gynaecology surgery and, to our knowledge, it will be the second largest RCT

*Correspondence:
Petra Baumann
petra.baumann@aesculap.de
Full list of author information is available at the end of the article

performed so far in total laparoscopic hysterectomy using unidirectional mid-term absorbable barbed suture materials.

Trial registration The study was prospectively registered before the enrolment of the first patient. Registration was performed under www.clinicaltrials.gov, NCT 06024109. Registered on 15 August, 2023.

Keywords Hysterectomy, Minimal invasive surgery, Laparoscopic surgery, Barbed suture, Knotless suture, Vaginal cuff closure

Background

Hysterectomy is one of the most performed surgical procedures worldwide in gynaecology [1]. The number of hysterectomy interventions in women aged 40 to 80 has steadily increased from 10 to 38 percent [2]. Reasons for a hysterectomy can be tumours, myomas, dysfunctional uterine bleeding and endometriosis [3, 4]. Total laparoscopic hysterectomy (TLH) has become the standard surgical method, whereby the number of robotic assisted surgeries is continuously increasing, especially in the United States [5]. Of all robotic-assisted procedures performed worldwide, gynaecology takes with 50% number one, followed by urology with 30% and general surgery with 20% [6].

A vaginal cuff dehiscence (VCD) presents a rare but severe complication after a hysterectomy. A late identified VCD can lead to life-threatening complications such as sepsis, peritonitis or bowel obstructions [7]. A VCD is defined as a complete or partial separation of the anterior and posterior edge of vaginal epithelium, with or without the presence of evisceration of intra-abdominal contents [8]. An increased risk for the development of a VCD has been described for laparoscopic compared to vaginal or open hysterectomy [9–12]. The overall VCD incidence after hysterectomy for benign indications is reported with 0.53% ranging from 0–3.5% [7]. Possible risk factors for the development of a VCD can be early resumption of sexual intercourse, smoking, reduced blood circulation, infection, thermal cutting and the morphology of the collagen structure [7, 8, 13].

The most challenging and time-consuming step during laparoscopic interventions is intracorporeal suturing and knotting [14, 15]. In recent years, barbed suture materials have been developed to facilitate and simplify suturing, and to avoid knotting [14, 15]. These knotless threads have been used in gynaecology since 2008 [16]. The benefits of this kind of suture material are as follows: no need for knot-tying, equal distribution of the tension along the wounds, secure approximation of the tissue, and no slippage [8, 14, 15, 17, 18]. Barbed sutures have been introduced in laparoscopic gynaecology to reduce operation time as well as intra- operative complications such as blood loss and postoperative complications such as vaginal cuff dehiscence [14, 19, 20].

To our knowledge, a total of 12 meta-analyses and systematic reviews have been performed in gynaecology so far (myomectomy, caesarean section, hysterectomy), which analysed the safety and effectiveness of barbed sutures [7, 8, 15, 21–29]. Of these, 5 meta-analyses have addressed the indication hysterectomy [7, 8, 21, 26, 29]. The outcome showed that barbed sutures are safe and effective, this type of suture material reduces operation time, suturing time for vaginal cuff closure, blood loss, surgical site infections and also lowers surgical difficulty, without an increase of hospital stay and postoperative complication rate in comparison to conventional sutures [8]. Furthermore, it was mentioned by several authors that the use of barbed sutures is a good option to decrease the rate of vaginal cuff dehiscence [7, 21, 26]. In addition, Iavazzo et al. reported a reduction of 2.4 min and Hafermann et al. of 4.84 min using barbs compared to conventional suture material for vaginal cuff closure after laparoscopic hysterectomy [8, 29]. An easy handling and a short learning curve were described by Siedhoff et al. for barbed sutures as well, due to the absence of knots, which facilitates the incorporeal handling of the suture material [19, 26, 30].

Various self-retaining sutures (V-Loc™, Quill SRS™, Stratafix™) are currently on the market. They differ in their configuration unidirectional versus bidirectional, in their absorption profile absorbable versus non-absorbable, in their anchoring element to fix the thread in the tissue (loop or anchor), and in the design and distribution of the barbs along the thread. They are available in different sizes and length/needle combinations.

These types of suture materials are nowadays commonly applied in various surgical interventions, including gynaecology [7, 8, 21–23, 25–27, 29], orthopaedics [31–38], urology [39–43], as well as in plastic [44] and general surgery [45–48].

Regarding the safety profile of barbed sutures, 6 cases of bowel obstructions have so far been reported in gynaecology with a causal relationship to the medical device [49–52]. Four cases were seen using knot-less sutures for peritoneal closure after sacral colpopexy [49, 50], one case after myomectomy and another one after hysterectomy [52, 53]. In all cases, the complication occurred due to the attachment of a too long free end of the barbed

suture to the ileum. This can be prevented by cutting the barbed suture flush to the tissue which minimises the length of the tail of suture to prevent intra-abdominal iatrogenic complications [52].

Only a few RCTs comparing the clinical outcome of self-anchoring sutures to conventional suture material for laparoscopic hysterectomy have been published [30, 53–55]. Most of them had a monocentric design, including a small sample size using either a unidirectional mid-term absorbable (V-Loc-90) or bidirectional long-term absorbable (Quill) barbed suture material for vaginal cuff closure after laparoscopic-/robotic-assisted hysterectomy.

Aim

The aim of our international, multicentric, randomised controlled, patient blinded, sample size powered BARHYSTER study is to assess the performance of a novel unidirectional mid-term absorbable barbed suture, which differs in its configuration from other barbed sutures to close the vaginal cuff after laparoscopic hysterectomy. Furthermore, the current study is the first study comparing two different mid-term absorbable self-anchoring sutures in gynaecological surgery.

Objective

This study is expected to confirm the hypothesis that the use of a novel unidirectional mid-term absorbable barbed suture can significantly reduce the time to close the vaginal cuff after total hysterectomy in comparison to conventional sutures (historical data from the literature). In addition, the study will prove as a secondary hypothesis the superiority of the novel unidirectional mid-term barbed suture to a competitor's unidirectional mid-term absorbable suture regarding the closure time for vaginal cuff approximation after TLH.

Methods/ design

Design and setting of the study

The current randomised, multicentric, single blinded, two-group parallel trial started in March 2024 in Germany and Spain and is still ongoing. End of recruitment is expected to be completed in the third quarter of 2025 and the 6-month follow-up examination and data collection will be finished until the second quarter of 2026. Patients are recruited in a consecutive manner in three hospitals, two in Germany (Krankenhaus Sachsenhausen, Frankfurt am Main and Bürgerhospital, Frankfurt am Main), and one in Spain (Hospital Sant Joan de Déu de Manresa, Barcelona). Ethics committees endorsed the study design prior to patient acquisition. Ethics approval was given by the responsible ethics committees (Ethik-Kommission bei der Landesärztekammer Hessen, Frankfurt am Main, Germany, project number: 2023–3261-evBO and Comité Ètic d'Investigació, Fundació Unió Catalana d'Hospitals, Barcelona, Spain, project number CEI 23/39). The study was prospectively registered in the international clinical trials platform of the World Health Organization at www.clinicaltrials.gov (NCT 06024109) before patient recruitment started. If modifications to the study protocols are necessary, an amendment will be set up by the Sponsor in cooperation and agreement with the principal investigators of the clinics and submitted to responsible ethics committees for approval. Modifications will not be implemented until the ethics committee have provided their approval.

As a short-title for this study – "Barbed suture for total hysterectomy" has been used. Therefore, as an acronym "BARHYSTER" has been chosen, which stands for BARbed sutures for HYSTERectomy.

A total of 132 patients will be randomly allocated in a 3:1 ratio to two different barbed suture groups to close the vaginal cuff after total laparoscopic hysterectomy (99 patients receiving the novel barbed suture material: 33 patients obtaining the competitor barbed suture material). There were some reasons to choose a 3:1 allocation ratio in favour of the experimental arm (novel unidirectional mid-term absorbable suture) compared to the control arm (competitor unidirectional barbed suture). The authors would like to generate more reliable clinical data to assess the safety and performance of the novel unidirectional barbed suture material compared to the control competitor unidirectional barbed suture, which has been analysed in several gynaecological studies in the past. Furthermore, the increase of the experimental group size also leads to an increase of the accuracy regarding the safety data, which can be illustrated by the "rule of 3". This rule states that if a certain complication did not occur in a sample of N, then the respective complication rate is less than 3/n (with 95% confidence). The basis of this rule is the good approximation of the upper limit of a 95% confidence interval for 0 events in N subjects for $N > 30$. Transferred to the current study design with an increased experimental group size, it means that a complication which does not occur in the experimental group should have a lower probability than 3/99 (approximately 3%).

The surgeons/gynaecologists participating in the study are experienced and well-trained in the performance of laparoscopic gynaecological procedures and familiar with the application of self-anchoring sutures in a 2-dimensional surgical field. Approximately 23,000 Bürgerhospital, 9,400 Krankenhaus Sachsenhausen patients are treated in the participating German hospitals, and 27,856 patients in the Spanish clinic; of these, 8,500 patients are operated in the German Department

of Gynaecology in the Bürgerhospital and 3,600 in the Krankenhaus Sachsenhausen, and 636 patients in the Spanish Department of Gynaecology per year, respectively. In the Spanish hospital, 50 laparoscopic hysterectomies are performed annually; 75 in the German hospital Krankenhaus Sachsenhausen and 10 in the Bürgerhospital. The clinics have been selected to exclude the learning curve with regard to laparoscopic procedures and the usage of barbed suture material.

The patients will be unaware of the barbed suture type applied for vaginal cuff closure until the end of the study. Before inclusion in the study, each participant will provide an informed consent. After surgery, an examination will take place at day of discharge, 6–8 weeks and 6 months postoperatively onsite at the hospital (Fig. 1, CONSORT Flow Chart) [56]. This time schedule has been selected because it reflects the daily practice of the hospital and the absorption of both suture materials is completed after 6 months postoperatively. The study will last in total 2 years (18 months recruitment plus 6 months follow-up). Our trial is reported in line with the SPIRIT Guideline, which is an international standard to publish study protocols [57]. The SPIRIT checklist is provided as an appendix and a study flow chart is also included (Fig. 2).

Characteristics of the participants and description of materials

Eligibility

Females at least 18 years of age scheduled for an elective minimal invasive total hysterectomy who provided written informed consent were eligible for participation.

The main inclusion criteria for the present study is the performance of a minimal invasive total hysterectomy, which includes laparoscopic as well as robotic assisted surgeries. Currently in all participating clinics the total hysterectomy is performed laparoscopically, but if the clinics decide in the running study to switch to robotic assisted surgeries, this would be possible and a subgroup analysis would be made regarding this subgroup population.

Exclusion criteria were as follows:

- Emergency surgery
- Open surgery
- Patient undergone immunosuppressive drug treatment within prior 6 months
- Patients with hypersensitivity or allergy to the suture material
- Participation in another RCT
- Non-compliance of the patient

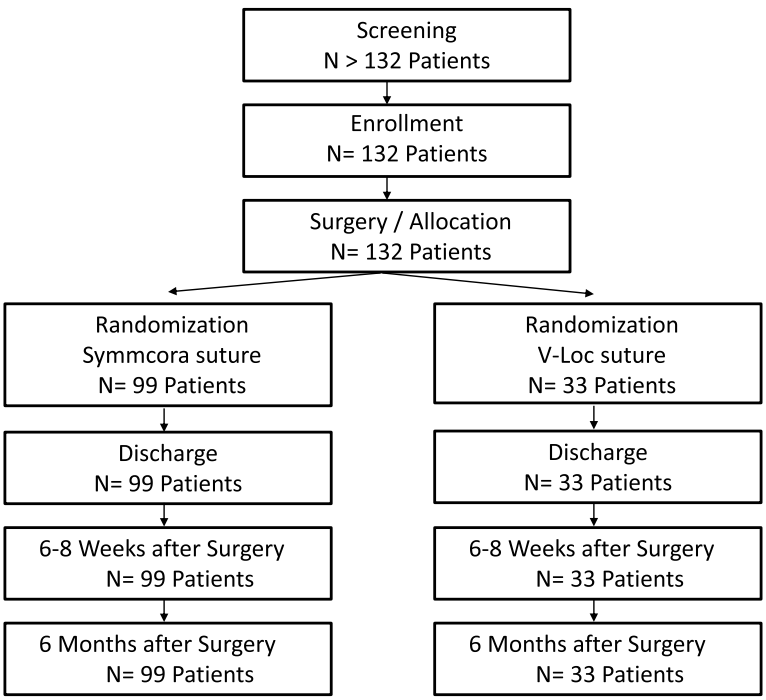

Fig. 1 CONSORT Flow-Chart BARHYSTER

	STUDY PERIOD					
	Enrolment	Allocation Day of surgery	Post-allocation			Close-out
TIMEPOINT**	*Approx. 1 - 2 months before surgery*	0	*Discharge*	*6-8 weeks*	*6 months ±2 weeks*	*6 months± 2 weeks*
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Demographics	X					
Medical History	X					
Allocation		X				
INTERVENTIONS:		X				
Barbed suture		X				
Competitor barbed suture		X				
ASSESSMENTS:						
Time for vaginal cuff closure		X				
Operation duration		X				
Handling of the suture material		X				
Pain	X		◆—	—	—◆	
Satisfaction			◆—	—	—◆	
QoL (EQ5D5L)	X			X	X	
FSFI	X			X	X	
Length of hospital stay			X			
AE/SAE (complications)		◆—	—	—	—◆	
Costs		X	X			

Fig. 2 SPIRIT diagram of BARHYSTER regarding the time schedule for enrolment, allocation, follow-up examination and assessment

Screening of patients for eligibility will be performed by a well-trained and experienced gynaecologist located in the Department of Gynaecology of the participating hospitals. Recruitment of the patients will be done a few weeks before they receive the planned elective surgical intervention.

Patients who meet the inclusion criteria in full will be asked for their willingness to participate in the BARHYSTER study and the physician will inform each patient verbally and by using written information about the study modalities. For each patient who agrees to participate, a written informed consent has to be obtained in advance before any study procedure takes place, in line with the origins of the Declaration of Helsinki and due to the German Data Protection Law (GDPR) which is applicable in Europe. The patients will be advised in the informed consent form that they have the right to withdraw from the study at any time without prejudice. Patients who prematurely terminate the participation in the trial will not be replaced. Their data will be analysed until their withdrawal of consent, or until their lost-to follow-up or the day when they prematurely terminated the study. Intra-drop-outs (e.g. conversion from laparoscopic to open setting) will be replaced in order to keep the planned sample size, because these patients will not be randomised. In any case (withdrawal, premature termination as well as scheduled termination) the study termination page of the CRF has to be completed and the reason for unscheduled termination has to be reported. Reasonable effort has to be made to contact any patient during the course of the study in order to complete assessments and to retrieve any outstanding data and study supplies in order to prevent a lost to follow- up. Before a patient is reported as "lost-to follow up", the patient should have been contacted three times by the clinic for respective follow-up examination.

Description of the suture material

Novel unidirectional mid-term absorbable suture—Symmcora® Mid-term (Experimental novel suture group-SBS-group) The barbed suture material investigated in the current study is named Symmcora® Mid-term and is manufactured by B.Braun Surgical SA, 08191 Rubi, Barcelona, Spain. It is a sterile synthetic, mid-term absorbable monofilament symmetric anchoring device made from a copolymer of 72% glycolide, 14% ε-caprolactone and 14% trimethylene carbonate, comprising an elongated main body (core) with anchoring elements that provide a knotless wound closure capacity to the device, intended for secure fixation in tissue without using knots. In the current study, the barbed suture material is used in its unidirectional configuration. Here, a single group of anchors is placed along the elongated body being the wound closure device provided with a locking system at the distal end, opposite to the longitudinal direction the anchors point to, see Fig. 3. The diameter refers to unbarbed section length near the needle attachment area. The diameter in the needle-attachment zone of $size_n$ is equivalent to the diameter of $size_{n+2}$ having the same USP designation.

Biocompatibility tests have shown that the unidirectional barbed suture is non-cytotoxic, non-mutagenic, non-genotoxic, non-toxic, non-pyrogenic, non-irritating, non-sensitizing and biocompatible. The suture tensile strength is 87% after 7 days and 51–57% after 14 days. Mass absorption of the device is essentially complete after approximately 90–120 days post-implantation.

Application Symmcora® mid unidirectional configuration is inserted in intact tissue directly above the apex in a direction away from the incision. In order to subsequently lock the locking system, it is recommended to insert it obliquely to the incision line. The device must be pulled through the tissue until resistance from the locking system is encountered. The locking system must be placed plane and visible above the tissue. To lock the locking system position, the first stitch must be passed above it. The device is then advanced to the other extreme of the incision according to a continuous suture pattern, taking apposing bites on either side of the wound in a standard fashion. To achieve the desired approximation and tension, the device is gently pulled on with each tissue passage.

After the placement is completed, either two passes in reverse direction across the incision or two additional bites of tissue lateral to the end of the incision are taken to lock the device in place. Finally, the device is cut flush with the surface of the tissue and care is taken to retain enough self-anchoring lengths to complete the device placement.

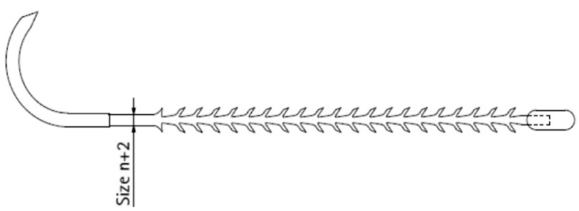

Fig. 3 Schematic drawing of the unidirectional configuration of the barbed thread Symmcora® Mid-term, (Source: B.Braun Surgical SA, Rubi, Barcelona, Spain)

Unidirectional mid-term barbed suture—V-Loc.™ 90 (Control competitor suture group- VBS-group) The control suture material is V-Loc™ 90 Absorbable Wound Closure Device manufactured by Medtronic, New Haven, CT, USA. [http://www.medtronic.com/covidien/products/wound-closure/barbed-sutures]. The absorbable wound closure device consists of a barbed absorbable thread armed with a surgical needle at one end and a loop end effector at the other. The barb and loop end effector design enable tissue approximation without the need to tie surgical knots. The sterile device is prepared from a synthetic copolymer composed of glycolide, diaxanone and trimethylene carbonate. The suture material presents dual-angle cut barbs which are distributed in a circumferential manner on the surface of the thread. USP designations for diameter are applicable to the absorbable wound closure device material prior to barbing. After the creation of barbs, the absorbable wound closure device is identified as one size smaller than the non-barbed suture. This modification reduces the tensile strength of the suture similar to the effect of knot tying in non-barbed suture. Therefore, the straight pull tensile strength of the V-Loc ™ 90 absorbable wound closure device is comparable to the USP knot pull strength for non-barbed suture of the equivalent size. Absorption of the device begins as a loss of tensile strength without appreciable loss of mass. After 7 days, the device has a 90% tensile strength and of 75% after 14 days. Animal data indicate that the absorption is essentially complete after 90 to 110 days. Progressive loss of tensile strength and absorption of the device occurs by means of hydrolysis, in which the device is broken down to glycolic acid, dioxanoic acid, propane diol and carbon dioxide which are subsequently absorbed and metabolized by the body.

Application To begin a continuous suture pattern, opposite bites on either side of the wound are taken in standard fashion. The V-Loc ™ 90 absorbable wound closure device is anchored by passing the needle end of the suture through the pre-formed loop end effector. Gentle traction on the suture anchors the suture and approximates the wound edges. Approximation of the tissue is done by using a continuous pattern taking care to overtighten the suture line while trailing. To end the suture line for deep tissues, 2 additional bites are taken beyond the terminal commissure to anchor the line. While applying gentle traction on the free end of the suture, the latter is cut flush with the surface of the tissue.

V-Loc ™ suture barbed suture material was selected as a comparator in the current study, because most of the published RCTs comparing barbed sutures versus conventional suture material have used V-Loc ™ as a comparator for vaginal cuff closure after TLH and therefore a lot of clinical data are available for comparison of our clinical outcome.

Description of process, interventions and comparison, outcomes

Process

An initiation visit was performed by the project management in each hospital before the start of the study to inform and instruct the medical staff involved on study-specific formulars and modalities. Reporting of the collected data is performed by the gynaecologist and nurses firstly on paper-based CRF and when transferred in a web-based eCRF owned by the Sponsor. To verify adherence to the study protocol and to perform source data verification, the entered data are checked on a regular basis by a research monitor. Any protocol violation will be clearly described and reported. To strength protocol adherence regarding the follow-up examinations, each patient receives a written appointment for the 6–8 weeks and 6 months follow-up visits by the study personnel on the day of discharge. For standardisation of the suture groups, suture material from the same batch was ordered and included in the opaque randomisation envelopes.

Allocation and randomisation

A computer-generated randomisation list distributing both suture groups in a 3 SBS:1 VBS ratio using different random block lengths unavailable for the clinic was prepared by the statistician of the Sponsor. To ensure concealment, the block size will not be disclosed. The randomisation list is kept and sealed at the Sponsor site. Therefore, the clinical staff has no influence on the randomisation result. A stratification is done by the centre to reduce centre-specific effects. For randomization, opaque sealed randomisation envelopes containing the information of the random allocation of the device, a randomization fax form as well as the respective suture material SBS or VBS in appropriate numbers, were prepared by the Sponsor and provided to the participating clinics in sufficient quantity. The randomisation envelopes are stored in the principal investigator office and individually transferred to the operation room for each surgery by the responsible surgeon/gynaecologist. Assignment will be performed in a chronological manner by the gynaecologist, in line with a consecutive random number placed outside on the envelope. Randomisation of the patient will take place intraoperatively. Briefly after the removal of the uterus, the nurse will open the envelope and mention the randomisation result to the operating team. To inform the Sponsor on time regarding the successful randomisation of a patient, a randomisation fax including

the result of the randomisation is sent by the clinic to the Sponsor after each surgery.

Blinding

To guarantee unbiased assessment of the primary endpoint and a valid assessment of the postoperative outcome judge by the patients, subjects and the data analyst will be blinded. The surgeons/gynaecologist cannot be blinded because the suture type can be differentiated by its configuration, and the surgeon must be aware of the suture material to perform the vaginal cuff closure. As far as the data base is closed and the analysis population has been determined, the statistician will be unblinded. Unblinding of the patient is not planned during the study, but can be performed in case of serious adverse events or an emergency that necessitates the knowledge of the suture group. Unblinded patients will stay in the study and analysed as planned. If the number of unblinded patients is too high, maybe a subgroup analysis has to be performed to compare blinded and unblinded subjects.

Intervention description

Total laparoscopic hysterectomy will be carried out as usual and according to the hospitals' standards. The vaginal cuff closure will be performed in the study participants using randomly either Symmcora® Mid-term or V-Loc ™ 90 in a 3:1 ratio. Both selected suture materials are approved and CE-marked. In addition, both devices are applied in their intended use.

Experimental novel suture group: Symmcora® Mid-term barbed suture (SBS) In the experimental novel suture group (SBS—group), one barbed thread of USP (2/0), either 15 cm or 30 cm, violet connected with a HR26 mm needle will be used to close the vaginal cuff. The application method is described under "Description of the suture material.

Control competitor suture group: V-Loc.™ 90 barbed suture (VBS) To perform the vaginal cuff closure in the control competitor suture group (VBS—group), a single thread of USP 2/0, 23 cm, violet combined with a GS-22 taper needle is used. Details regarding the application method can be found under "Description of the suture material".

Intraoperative documentation includes the initials and position of the surgeon, the randomisation result (SBS or VBS) and the modalities of the surgery: only hysterectomy, hysterectomy with lymphadenectomy, hysterectomy with salpingectomy (unilateral or bilateral), hysterectomy with oophorectomy (unilateral or bilateral). In addition, the following parameters are also mandatory, and recorded and measured in all randomised patients during surgery:

- total operation time
- suturing time to perform the vaginal cuff closure
- number of suture stitches
- length of the remaining suture material
- length of the vaginal cuff incision
- single layer or double layer closure of the vaginal cuff tissue
- weight of the uterus
- presence of intra-abdominal adhesions
- classification of the tumour (only applicable for tumour patients)
- handling properties of the applied suture type
- estimated blood loss
- intraoperative blood transfusion
- antibiotic prophylaxis
- device malfunction
- adverse events

Patients will be prematurely discontinued from the study if the decision is made intraoperatively by the surgeon to convert from laparoscopic setting to open. In that case, the randomisation envelope will not be opened and the indicated suture material will not be applied.

Outcomes

Data will be collected preoperatively (baseline characteristics, eligibility), intraoperatively, on the day of discharge, 6–8 weeks and 6 months after surgery. Figure 2 lists the primary and secondary outcomes depending on the time schedule.

Primary endpoint The primary objective of the study is the time needed to perform the vaginal cuff closure in minutes after laparoscopic TLH using a stop watch. The time starts when the needle passes the tissue the first time and ends after completion of the wound closure (cutting the needle from the thread).

Secondary outcomes The following *safety parameters* will be raised until the end of the study and reported as adverse events:

- Vaginal cuff infection
- Vaginal cuff dehiscence (defined as a visually confirmed partial or complete opening of the vaginal stump with or without visceral organ herniation)
- Vaginal cuff granulation formation
- Pelvic abscess formation
- Fever > 38 °C within 48 h

- Hematoma
- Vaginal spotting (defined as bloody vaginal discharge that did not require extraordinary procedures or medication and disappeared spontaneously. (Days of postoperative bleeding, number of pads/tampons used)
- Vaginal bleeding (defined as postoperative vaginal stump bleeding that required additional stump suture to stop bleeding. (Days of postoperative bleeding, number of pads/tampons used)
- Urinary tract infection
- Bladder injury
- Ureter injury
- Bowel obstruction
- Ileus
- Cystitis
- Pelvic adhesions

Documentation of intra-operative suture issues will be also performed and reported as adverse device events:

- Suture rupture
- Needle bending
- Disconnection between the needle and the thread
- Disconnection between the anchor and the residual barbed suture
- Any suture-related complication

Furthermore, the length of hospital stay, duration of surgery, patient satisfaction, costs, pain, quality of life and suture handling properties will be compared in both suture groups. Duration of hospital stay is defined as the period from day of surgery until day of discharge. Evaluation of costs includes the cost of the suture material, cost per operation minute, number of threads and the cost per hospital day. The Visual Analogue Scale (VAS) is a numeric scale ranging from 0 (low) to 100 (high) used for pain assessment performed by the patient. In addition, patients will judge their satisfaction using a numeric scale ranging from 0 (not satisfied) to 100 (highly satisfied). Analysis of quality of life will be performed using the EQ5D5L questionnaire, which is a standard to measure the health status developed by the EuroQoL Group to provide a simple, generic measure of health for clinical and economic appraisal [58]. The questionnaire consists of a descriptive system comprising 5 dimensions (mobility, self-care, usual activities, pain or discomfort, anxiety or depression) and the EQ Visual Analogue Scale (EQ-VAS). Each dimension has five levels: no problem, slight problems, moderate problems, severe problems, and extreme problems. Using the EQ-VAS, each patient records her healthy status ranging from 0 (the worst health you can imagine) to 100 (best health you can imagine). The EQ5D5L is used in the German and Spanish language and a license has been obtained by the Sponsor from EuroQol-Group.

Furthermore, the Female Sexual Function Index (FSFI), which is a simple, objective, valid, reliable and standardised self-assessment tool to analyse and report the outcome of female sexual function within the last 4 weeks is filled out by the patients [59, 60]. The FSFI is a questionnaire which consists of 6 domains (desire, arousal, lubrication, orgasm, satisfaction, pain) including in total 19 items/questions. Except for 4 items, all other items can be scored with a 0–5-point Likert scale, the other four items with a 1–5-point Likert scale. Higher scores indicate greater levels of sexual functioning of the respective item/domain. The sum of each domain score is multiplied by a certain domain factor ratio (0.6 desire, 0.3 arousal, 0.3 lubrication, 0.4 orgasm, 0.4 satisfaction, 0.4 pain) and summed up to a total score, whereby the total score can range from a minimum of 2.0 to a maximum of 36. The FSFI is used in the Spanish and German version and a license for usage has been ordered by the Sponsor [61, 62].

The handling of the suture material will be assessed by the participating gynaecologist after each surgery using a questionnaire including different categories with 5 evaluation levels (strongly agree, agree, neither, disagree, strongly disagree) and the outcome for both suture types (SBS vs VBS) will be compared.

Data management / safety data monitoring board / audit

Patient baseline data and outcome variables will be collected by the local investigators from the patient file and entered in an eCRF provided by the Sponsor. The EQ5D5L and FSFI self-assessment questionnaire will be filled out by the patients themselves and the reported data will be transferred from paper to the eCRF platform by the clinical personnel. The eCRF is only accessible for the local investigator and password protected. Data will be checked for completeness, correctness, plausibility and consistency by validated programs.

Patient data will be handled confidentially and subjected to the Data Protection Law (EU GDPR). The informed consent form and the questionnaires containing personal data will be stored safely in a file placed in the principal investigator office during the study, which is protected against unauthorised access to keep the confidentiality of the data. The collected data will be securely stored for 15 years after study completion.

Since the study analyses two approved suture materials applied in their intended use and neither invasive nor additional burdensome measures are performed, a

Data Safety Monitoring Board is not established and an interim analysis will not be conducted before study completion. Audits are also not planned, because the study is performed in routine clinical settings.

Monitoring

On-site monitoring visits will be performed regularly as defined in the monitoring plan and dependent on the number of included patients per clinic by a qualified authorised representative of the Sponsor to ensure study protocol adherence and data accuracy, to perform source data verification, to protect patient rights, to assist the investigator in study-related activities and to assess the performance of the participating sites. Therefore, the centres allow and provide the monitor with access to source data and documents. For these patients, an informed consent will also be obtained. In the case of missing data and inconsistencies, these will be clarified with the responsible investigator. After each monitoring visit, a monitoring report will be created by the monitor to summarise the documents reviewed, discrepancies, findings, deviations and action taken or recommended.

Adverse events reporting

The Principal Investigator of each clinic will collect all adverse events (AE), serious adverse events (SAE), and device deficiencies (DD) occurring during the study and will report them within 24–48 h to the Sponsor by using the AE/SAE/DD form which is integrated in the eCRF form. In addition, for each event seriousness, intensity, expectedness (expected/unexpected), causal relationship with the device or with the surgical procedure have to be assessed and recorded, including the measure taken as well as the outcome of each event. All serious adverse events with a suspected or proven causal relationship with the experimental suture material will be reported to the product complaint management of the Sponsor according to the vigilance process. All serious adverse events occurring with a causal relationship to the competitor product will be reported by the clinic to the manufacturer as complaints. All events occurring until the patient's 6-month follow-up examination will be reported and ongoing events will be followed up until 28 days following the patient's last visit.

All complications appearing during the study will be treated according to the clinic's treatment protocol.

Statistical analysis and sample size calculation

Sample size calculation

The sample size calculation is based on an efficacy endpoint "time to perform the vaginal cuff closure" to demonstrate superiority of the novel unidirectional mid-term absorbable barbed suture (SBS) compared to a historical conventional control from the literature as well as the superiority of the novel unidirectional mid-term absorbable barbed suture (SBS) compared to a competitor unidirectional barbed suture (VBS). Therefore, the primary analysis consists of testing a two-step hierarchical hypothesis system, which allows for an ordered test procedure without inflating the type 1 error [63]. The step two of the procedure only takes place when step one succeeds rejecting the null hypothesis (one-sided $p < 0.025$), see Fig. 4.

Several studies have been published investigating barbed suture materials versus conventional suture materials for vaginal cuff closure after hysterectomy. The weighted group means and the weighted pooled standard deviations were calculated based on the results of the sub-set of three studies providing suturing times for vaginal cuff closure using a unidirectional barbed suture versus a conventional suture material [30, 53, 64]. The calculation showed a mean weighted closure time of 13.9 ± 6.3 min for the conventional suture material and this value was used for historical comparison. Furthermore, a mean weighted closure time of 11.8 min was calculated for the unidirectional barbed suture material based on these three studies. For the novel unidirectional barbed suture material (SBS), we expected a faster closure time of 9 min because of the different anchoring configuration compared to the control competitor unidirectional barbed suture material (VBS).

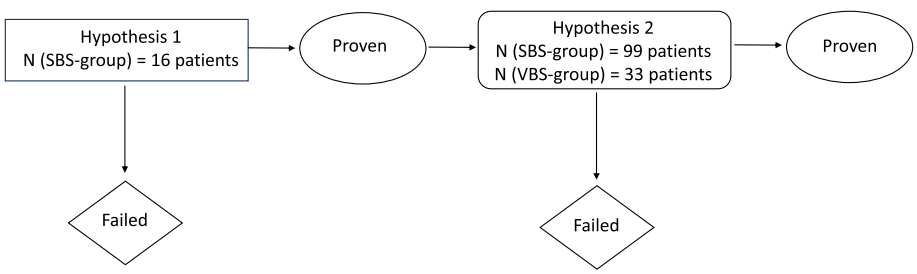

Fig. 4 Hierachical hypothesis testing order within BARHYSTER study

1. Hierarchical hypothesis 1: Comparison to historical literature data

   Considering 9 minutes in the experimental novel unidirectional barbed group (SBS) for vaginal cuff closure compared to 13.9 minutes for the historical conventional control group from the literature, a sample size of 16 patients will have 80% power to reject the hypothesis described below, assuming that the standard deviation is 6.3 minutes, using an one-sided one sample t-test with a 0.025 one-sided significance level.

   H0: $\mu \geq \mu 0$

   μ (experimental novel barbed suture group (SBS) mean), $\mu 0$ (historical conventional suture control group from the literature)
2. Hierarchical hypothesis 2: Randomised controlled comparison SBS vs. VBS
   The second hypothesis of the study is to show that the experimental novel mid-term unidirectional suture (SBS) is superior compared to the control competitor unidirectional mid-term absorbable suture (VBS) regarding the time to close the vaginal cuff.
   H0: $\mu 1 \geq \mu 2$
   $\mu 1$ (experimental novel unidirectional barbed suture group (SBS) mean), $\mu 2$ (control competitor unidirectional barbed group (VBS) mean)
   A sample size of 132 patients will have 80%power to prove the difference between the experimental novel barbed suture group (SBS, $\mu 1 = 9$ min.) and VBS group (control competitor barbed suture group, $\mu 2 = 11.8$ min.) assuming respective standard deviations of 4.45 min. and 5 min., using a two-group t-test with a 0.05 two-sided significance level. The Satterthwaite method will be used for the test.

Hierarchical hypotheses testing order (figure 4) If hypothesis 1 fails, hypothesis 2 is also considered failed. If hypothesis 1 is proven, hypothesis 2 will also be tested to full two-sided level of 5% without inflating the type 1 error rate.

The sample size of the experimental novel barbed suture group (SBS) including a total of 99 patients is sufficient for testing hypothesis 1 (n=16 patients) and hypothesis 2.

No adjustment for drop-outs is made because the primary endpoint will be measured intra-operatively and intra-operative drop-outs will be replaced to achieve the sample size.

For sample size calculation, SAS Viya, software version 4.00, SAS Institute Inc., Cary NC, USA, was used.

Statistical methods and analysis

Secondary variables will be analysed using standard procedures as appropriate. For identification of relevant influencing factors and parameters of primary and secondary variables, multivariate regression models may be used where appropriate. Depending on the outcome variable, linear or logistic models may be implemented. In these models, patient age, sex, BMI and the respective baseline value will be used as covariates to adjust for.

For data analysis, the intention-to-treat-principle will be applied. To graphically present the eligibility, allocation and follow-up process of the subjects, a CONSORT flow chart will be provided. Baseline and demographic data will be shown as min., max., median, means with standard deviation, or absolute and relative frequencies as appropriate. The test regarding the primary variable is considered confirmatory, all other tests are explanatory and secondary variables will be analysed descriptively. For binary data, a Chi-Square test will be performed; for non-parametric data, a U test according to Wilcoxon-Mann–Whitney or to Kruskal–Wallis and a t-test or One-Way-ANOVA for metric data, if a normal distribution is assumed.

Missing data will be analysed as such and will not be replaced by estimates. All eligible patients who obtained the intended study treatment will be included in the analysis. Patients violating the inclusion or/and exclusion criteria will be dropped out from the study and deviations from the study protocol and judged as protocol violation. The safety analysis is performed according to the as-treated principle.

The analysis will be performed after the completion of the 6-month follow-up. An interim analysis is not planned.

Disseminations plan

The outcome of the study will be published in a peer-reviewed international journal and the results will be also presented in international and national conferences.

Discussion

In recent years, the number of minimal invasive hysterectomies, especially robotic-assisted procedures, have increased [5, 6]. To ensure a secure and efficient clinical outcome, new surgical techniques and devices have been developed. During minimal invasive surgery, the most time-consuming and challenging step is the intracorporeal suturing and knotting [14, 15]. The usage of barbed sutures facilitates and simplifies suturing, avoids knotting, equally distributes the tension along the suturing

line, leads to a secure tissue approximation and prevents suture slipping [8, 14, 15, 17, 18]. It has been shown that barbed sutures are safe and well-tolerated by the patients [65]. Furthermore, this type of suture material shortens the time for vaginal cuff closure leading to less costs compared to conventional suture material without an increase of the complication rates [8, 65]. An easy handling as well as a short learning curve have been also described for barbed sutures [7, 19, 30, 65].

Bowel obstructions which have been observed in the initial period of barbed suture application can be omitted by cutting the barbed thread flush to the tissue [49–53].

Therefore, barbed sutures are an innovative and efficient alternative to conventional suture materials, but due to their higher manufacturing costs they are more expensive than traditional suture materials. In addition, surgeons need training courses to adapt their skills to the handling of this innovative suture material, but the learning curve is fast.

Currently, the following unidirectional absorbable barbed sutures are commercially available which differ in their configuration [66]. Unidirectional V-Loc™ (Medtronic, New Haven, CT, USA) has a loop at one end of the suture material which is used to fix the suture material in the tissue by passing the needle through the loop, and along the thread there are unique dual angle cut barbs in a circumferential fashion that anchor the suture to the tissue [67]. Stratafix™, (Johnson & Johnson, New Brunswick, NJ, USA) is available in two variations, in a symmetrical and a spiral design. The spiral version has a helical distribution of single-angle cut barbs along the suture material and an anchor at one end, which is used to fix the suture material to the tissue. The symmetrical version has mirror image barbs on both sides of the suture axis and is also combined with an anchor on one side [68]. Compared to the V-Loc™ suture material, it was described that the barbs of Stratafix™ are manufactured with a higher cut angle and with a deeper cut depth [66]. The barbs of unidirectional Quill™ SRS (Corza Medical, Westwood, MA, USA) are arranged in a spiral fashion along the suture and an adjustable loop design allows for an easy needle placement [69].

The novel barbed suture named Symmcora® manufactured by B. Braun Surgical SA, Spain, which is not yet available on the market, has in its unidirectional design an anchor at one side to fix the thread in the tissue and the barbs are arranged in a symmetrical manner along the thread to anchor the suture to the tissue and to approximate the wound.

The current BARHYSTER study will:

- analyse a novel unidirectional mid-term absorbable barbed suture material in gynaecological surgery.
- provide clinical evidence on level 1b due to its high-quality study design.
- compare for the first time the clinical outcome of two unidirectional mid-term absorbable barbed sutures, which differ in their design (loop versus anchor, spiral versus symmetrical barbs distribution along the thread), for vaginal cuff closure after laparoscopic hysterectomy.

Abbreviations

AE	Adverse event
BARHYSTER	BARbed suture for HYSTERectomy
CRF	Case Report Form
DD	Device Deficiency
eCRF	Electronic Case Report Form
EQ-5D-5L	Euro Quality of Life Questionnaire
FSFI	Female Sexual Function Index
GDPR	General Data Protection Regulation
Max.	Maximum
Min	Minimum
SAE	Serious Adverse Event
SBS	Symmcora Barbed Suture-group
TLH	Total Laparoscopic Hysterectomy
USP	United States Pharmacopoeia
VAS	Visual Analogue Scale
VBS	V-Loc Barbed Suture-group
VCD	Vaginal Cuff Dehiscence

Acknowledgements
The authors would like to thank Viktor Breul, the trial statistician responsible for sample size calculation who will perform the statistical analysis of the data after study completion. Thanks are due to the medical staff of the clinics involved in the study for their support in recruiting patients and data collection. Special thanks to all patients for their willingness to participate in the current trial.

Authors' contributions
PB set up the study proposal and wrote the study protocol. PB contributed to study design and is the lead trial methodologist. AH is the Chief Investigator and led the study. LHS, NGG, LS and AH were actively involved in patient recruitment and conducted the follow-up examination. The surgical interventions were done by AH, NGG and LHS. PB wrote the manuscript and all authors read and approved the manuscript.

Funding
B. Braun Surgical SA, Spain funded and sponsored the trial. The suture material needed to perform the clinical trial was provided by the Sponsor, was part of the financial support and concluded in a contract between the Sponsor and the clinics. The effort for data collection, documentation and reporting in the CRF is reimbursed by the Sponsor. In addition, the Sponsor has taken over the costs arising from EC approval and will pay the costs for open access publication. The Medical Scientific Department of Aesculap AG, Tuttlingen, Germany has taken over the responsibility for project management, monitoring, data management, statistical analysis and medical writing and acts like a clinical research organisation.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
An ethics approval was obtained from the responsible ethics committees in Germany and in Spain before patient recruitment started. For the Spanish Clinic (Comité Ètic d'Investigació de la Fundació Unió Catalana Hospitals, Barcelona, Spain, project number CEI 23/39, approval date 18 April 2023) and

German clinic (Ethics Committee "Ethik-Kommission bei der Landesärztekammer Hessen, Frankfurt am Main, Germany, project number: 2023–3261-evBO, approval date 17 June 2023). Before participation in the study, all included patients will provide their written informed consent. The study is carried out in line with the principles of the Declaration of Helsinki and in compliance with Good Clinical Practice. The Data Protection Law applies and the clinics will ensure the preservation of the pseudonymisation of the participants by using a unique patient identification and randomisation code. The study protocol is written in accordance with the recommendations of the Consolidated Standards of Reporting Trials (CONSORT) and SPIRIT guidelines. The SPIRIT checklist is provided as additional file.

Consent for publication

Each participant will provide a written informed consent that her anonymised data can be used for publications in scientific journals. Images or videos of individual participants will not be created and used.

Competing interest

PB is an employer of Aesculap AG. Amadeus Hornemann gives annual surgery courses for Aesculap AG. The other authors declare no competing interest.

Author details

[1]Department of Medical Scientific Affairs, Aesculap AG, Tuttlingen, Germany. [2]Department of Gynaecology, Hospital Sant Joan de Déu de Manresa, Manresa, Barcelona, Spain. [3]Department of Obstetrics and Gynaecology, Krankenhaus Sachsenhausen, Frankfurt Am Main, Germany. [4]Department of Operative Gynaecology, Frankfurt Am Main, Germany.

Received: 15 October 2024 Accepted: 4 December 2024
Published online: 14 January 2025

References

1. Wu JM, Wechter ME, Geller EJ, Nguyen TV, Visco AG. Hysterectomy rates in the United States, 2003. Obstet Gynecol. 2007;110(5):1091–5.
2. Hysterektomie | GBE kompakt 1/2014 (rki.de)
3. Hysterectomy - Why it's necessary - NHS (www.nhs.uk)
4. Smith K, Caceres A. Vaginal Cuff Closure in Minimally Invasive Hysterectomy: A Review of Training, Techniques, and Materials. Cureus. 2017;9(10): e1766.
5. ACOG.Commitee Opinion No. 444; 2009.Obstet Gynecol 114:1091–1095.
6. Bauer EC, Scholz C, Schochter F, De Gregoriod N, Janni W, Widschwendter P. Hysterektomie – operative Innovationen in der Gynäkologie am Beispiel einer „alten" Operation. Gynakologe. 2018;51:755–63.
7. Uccella S, Zorzato PC, Kho RM. Incidence and Prevention of Vaginal Cuff Dehiscence after Laparoscopic and Robotic Hysterectomy: A Systematic Review and Meta-analysis. J Minim Invasive Gynecol. 2021;28(3):710–20.
8. Iavazzo C, Mamais I, Gkegkes ID. The Role of Knotless Barbed Suture in Gynecologic Surgery: Systematic Review and Meta-Analysis. Surg Innov. 2015;22(5):528–39.
9. Uccella S, Ghezzi F, Mariani A, Cromi A, Bogani G, Serati M, Bolis P. Vaginal cuff closure after minimally invasive hysterectomy: our experience and systematic review of the literature. Am J Obstet Gynecol. 2011;205(2):119. e1–12.
10. Uccella S, Ceccaroni M, Cromi A, Malzoni M, Berretta R, De Iaco P, Roviglione G, Bogani G, Minelli L, Ghezzi F. Vaginal cuff dehiscence in a series of 12,398 hysterectomies: effect of different types of colpotomy and vaginal closure. Obstet Gynecol. 2012;120(3):516–23.
11. Ceccaroni M, Berretta R, Malzoni M, Scioscia M, Roviglione G, Spagnolo E, Rolla M, Farina A, Malzoni C, De Iaco P, Minelli L, Bovicelli L. Vaginal cuff dehiscence after hysterectomy: a multicenter retrospective study. Eur J Obstet Gynecol Reprod Biol. 2011;158(2):308–13.
12. Hur HC, Donnellan N, Mansuria S, Barber RE, Guido R, Lee T. Vaginal cuff dehiscence after different modes of hysterectomy. Obstet Gynecol. 2011;118(4):794–801.
13. Landeen LB, Hultgren EM, Kapsch TM, Mallory PW. Vaginal cuff dehiscence: a randomized trial comparing robotic vaginal cuff closure methods. J Robot Surg. 2016;10(4):337–41.
14. Greenberg JA. The use of barbed sutures in obstetrics and gynecology. Rev Obstet Gynecol. 2010 Summer;3(3):82–91.
15. Greenberg JA, Goldman RH. Barbed suture: a review of the technology and clinical uses in obstetrics and gynecology. Rev Obstet Gynecol. 2013;6(3–4):107–15.
16. Greenberg JA, Einarsson JI. The use of bidirectional barbed suture in laparoscopic myomectomy and total laparoscopic hysterectomy. J Minim Invasive Gynecol. 2008;15(5):621–3.
17. Kim JH, Byun SW, Song JY, Kim YH, Lee HJ, Park TC, Lee KH, Hur SY, Park JS, Lee SJ. Barbed versus conventional 2-layer continuous running sutures for laparoscopic vaginal cuff closure. Medicine (Baltimore). 2016;95(39): e4981.
18. Alessandri F, Remorgida V, Venturini PL, Ferrero S. Unidirectional barbed suture versus continuous suture with intracorporeal knots in laparoscopic myomectomy: a randomized study. J Minim Invasive Gynecol. 2010;17(6):725–9.
19. Siedhoff MT, Yunker AC, Steege JF. Decreased incidence of vaginal cuff dehiscence after laparoscopic closure with bidirectional barbed suture. J Minim Invasive Gynecol. 2011;18(2):218–23.
20. Medina BC, Giraldo CH, Riaño G, Hoyos LR, Otalora C. Barbed suture for vaginal cuff closure in laparoscopic hysterectomy. JSLS. 2014;18(1):83–8.
21. Bogliolo S, Musacchi V, Dominoni M, Cassani C, Gaggero CR, De Silvestri A, Gardella B, Spinillo A. Barbed suture in minimally invasive hysterectomy: a systematic review and meta-analysis. Arch Gynecol Obstet. 2015;292(3):489–97.
22. Agarwal S, D'Souza R, Ryu M, Maxwell C. Barbed vs conventional suture at cesarean delivery: A systematic review and meta-analysis. Acta Obstet Gynecol Scand. 2021;100(6):1010–8.
23. Gardella B, Dominoni M, Iacobone AD, De Silvestri A, Tinelli C, Bogliolo S, Spinillo A. What Is the Role of Barbed Suture in Laparoscopic Myomectomy? A Meta-Analysis and Pregnancy Outcome Evaluation. Gynecol Obstet Invest. 2018;83(6):521–32.
24. Khanuja K, Burd J, Ozcan P, Peleg D, Saccone G, Berghella V. Suture type for hysterotomy closure: a systematic review and meta-analysis of randomized controlled trials. Am J Obstet Gynecol MFM. 2022;4(6): 100726.
25. Raischer HB, Massalha M, Iskander R, Izhaki I, Salim R. Knotless Barbed versus Conventional Suture for Closure of the Uterine Incision at Cesarean Delivery: A Systematic Review and Meta-analysis. J Minim Invasive Gynecol. 2022;29(7):832–9.
26. Tulandi T, Einarsson JI. The use of barbed suture for laparoscopic hysterectomy and myomectomy: a systematic review and meta-analysis. J Minim Invasive Gynecol. 2014;21(2):210–6.
27. Zhang Y, Ma D, Li X, Zhang Q. Role of Barbed Sutures in Repairing Uterine Wall Defects in Laparoscopic Myomectomy: A Systemic Review and Meta-Analysis. J Minim Invasive Gynecol. 2016;23(5):684–91.
28. Riemma G, De Franciscis P, La Verde M, Ravo M, Fumiento P, Fasulo DD, Della Corte L, Ronsini C, Torella M, Cobellis L. Impact of the hemostatic approach after laparoscopic endometrioma excision on ovarian reserve: Systematic review and network meta-analysis of randomized controlled trials. Int J Gynaecol Obstet. 2023;162(1):222–32.
29. Hafermann J, Silas U, Saunders R. Efficacy and safety of V-Loc™ barbed sutures versus conventional suture techniques in gynecological surgery: a systematic review and meta-analysis. Arch Gynecol Obstet. 2024;309(4):1249–65.
30. Einarsson JI, Cohen SL, Gobern JM, Sandberg EM, Hill-Lydecker CI, Wang K, Brown DN. Barbed versus standard suture: a randomized trial for laparoscopic vaginal cuff closure. J Minim Invasive Gynecol. 2013;20(4):492–8.
31. Sun C, Chen L, Du R, Wu S, Ma Q, Cai X. Barbed Sutures in Total Knee Arthroplasty: A Meta-analysis of Randomized-Controlled Trials. J Knee Surg. 2021;34(14):1516–26.
32. Meena S, Gangary S, Sharma P, Chowdhury B. Barbed versus standard sutures in total knee arthroplasty: a meta-analysis. Eur J Orthop Surg Traumatol. 2015;25(6):1105–10.
33. Han Y, Yang W, Pan J, Zeng L, Liang G, Lin J, Luo M, Guo D, Liu J. The efficacy and safety of knotless barbed sutures in total joint arthroplasty: a meta-analysis of randomized-controlled trials. Arch Orthop Trauma Surg. 2018;138(10):1335–45.
34. Zhang W, Xue D, Yin H, Xie H, Ma H, Chen E, Hu D, Pan Z. Barbed versus traditional sutures for wound closure in knee arthroplasty: a systematic review and meta-analysis. Sci Rep. 2016;25(6):19764.
35. Borzio RW, Pivec R, Kapadia BH, Jauregui JJ, Maheshwari AV. Barbed sutures in total hip and knee arthroplasty: what is the evidence? A meta-analysis Int Orthop. 2016;40(2):225–31.

36. Xin WQ, Zhao Y, Wang H, Wu J, Wang HY, Gao YK, Yang XY. A better strategy using barbed sutures for wound closure in total knee arthroplasty. J Comp Eff Res. 2019;8(10):799–814.
37. Zhan ZL, Xin YM, Li HM, Sun CJ. Efficacy and safety of barbed sutures in total hip arthroplasty and total knee arthroplasty: a meta-analysis. Zhonghua Yi Xue Za Zhi. 2019;99(30):2375–82.
38. Li P, Zhang W, Wang Y, Li J, Yan P, Guo S, Liu J, Yang K, He Z, Qian Y. Barbed suture versus traditional suture in primary total knee arthroplasty: A systematic review and meta-analysis of randomized controlled studies. Medicine (Baltimore). 2020;99(21): e19945.
39. Lin YF, Lai SK, Liu QY, Liao BH, Huang J, Du L, Wang KJ, Li H. Efficacy and safety of barbed suture in minimally invasive radical prostatectomy: A systematic review and meta-analysis. Kaohsiung J Med Sci. 2017;33(3):107–15.
40. Bai Y, Pu C, Yuan H, Tang Y, Wang X, Li J, Wei Q, Han P. Assessing the Impact of Barbed Suture on Vesicourethral Anastomosis During Minimally Invasive Radical Prostatectomy: A Systematic Review and Meta-analysis. Urology. 2015;85(6):1368–75.
41. Lin Y, Liao B, Lai S, Huang J, Du L, Wang K, Li H. The application of barbed suture during the partial nephrectomy may modify perioperative results: a systematic review and meta-analysis. BMC Urol. 2019;19(1):5.
42. Li H, Liu C, Zhang H, Xu W, Liu J, Chen Y, Li T, Li B, Wu Z, Xia T. The Use of Unidirectional Barbed Suture for Urethrovesical Anastomosis during Robot-Assisted Radical Prostatectomy: A Systematic Review and Meta-Analysis of Efficacy and Safety. PLoS ONE. 2015;10(7): e0131167.
43. Zhan H, Huang C, Li T, Yang F, Cai J, Li W, Mao Y, Zhou X. The Self-Retaining Barbed Suture for Parenchymal Repair in Laparoscopic Partial Nephrectomy: A Systematic Review and Meta-Analysis. Surg Innov. 2019;26(6):744–52.
44. Su X, Lin Y, Wu Y, Feng K, Xiang N, Hu Z, Zhou J, Guo Q, Chen Z, Liao G, Du L, Huang J. Effectiveness and safety of knotless barbed sutures in cosmetic surgery: A systematic review and meta-analysis. J Plast Reconstr Aesthet Surg. 2023;87:416–29.
45. Velotti N, Manigrasso M, Di Lauro K, Vertaldi S, Anoldo P, Vitiello A, Milone F, Musella M, De Palma GD, Milone M. Barbed suture in gastro-intestinal surgery: A review with a meta-analysis. Surgeon. 2022;20(2):115–22.
46. Lin Y, Long Y, Lai S, Zhang Y, Guo Q, Huang J, Du L. The Effectiveness and Safety of Barbed Sutures in the Bariatric Surgery: a Systematic Review and Meta-analysis. Obes Surg. 2019;29(6):1756–64.
47. Wiggins T, Majid MS, Markar SR, Loy J, Agrawal S, Koak Y. Benefits of barbed suture utilisation in gastrointestinal anastomosis: a systematic review and meta-analysis. Ann R Coll Surg Engl. 2020;102(2):153–9.
48. Chaouch MA, Kellil T, Taieb SK, Zouari K. Barbed versus conventional thread used in laparoscopic gastric bypass: a systematic review and meta-analysis. Langenbecks Arch Surg. 2021;406(4):1015–22.
49. Quibel S, Roman H, Marpeau L. V-LOC…clusion [Volvulus following barbed suture]. Gynecol Obstet Fertil. 2012;40(6):382–3.
50. Vahanian SA, Finamore PS, Lazarou G. Delayed small bowel obstruction after robotic-assisted sacrocolpopexy. Female Pelvic Med Reconstr Surg. 2015;21(1):e11–3.
51. Burchett MA, Mattar SG, McKenna DT. Iatrogenic intestinal and mesenteric injuries with small bowel volvulus following use of barbed suture during laparoscopic myomectomy. J Laparoendosc Adv Surg Tech A. 2013;23(7):632–4.
52. Donnellan NM, Mansuria SM. Small bowel obstruction resulting from laparoscopic vaginal cuff closure with a barbed suture. J Minim Invasive Gynecol. 2011;18(4):528–30.
53. López CC, Ríos JFL, González Y, Vásquez-Trespalacios EM, Serna D, Arango A, Cifuentes C, Vásquez R, Castañeda JD, Almanza LA, Jiménez LA. Barbed Suture versus Conventional Suture for Vaginal Cuff Closure in Total Laparoscopic Hysterectomy: Randomized Controlled Clinical Trial. J Minim Invasive Gynecol. 2019;26(6):1104–9.
54. Ardovino M, Castaldi MA, Fraternali F, Ardovino I, Mosca L, Colacurci N, Signoriello G, Cobellis L. Bidirectional barbed suture in total laparoscopic hysterectomy and lymph node dissection for endometrial cancer: technical evaluation and 1-year follow-up of 61 patients. J Laparoendosc Adv Surg Tech A. 2013;23(4):347–50.
55. Tsafrir Z, Palmer M, Dahlman M, Nawfal AK, Aoun J, Taylor A, Fisher J, Theoharis E, Eisenstein D. Long-term outcomes for different vaginal cuff closure techniques in robotic-assisted laparoscopic hysterectomy: A randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2017;210:7–12.
56. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krle A-Jerić K, Hrobjartsson A, Mann H, Dickersin K, Berlin JA, Dore CJ, Parulekar WR, Summerskill WS, Groves T, Schulz KF, Sox HC, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: defining standard protocol items for clinical trials. Rev Panam Salud Publica. 2015;38(6):506–14.
57. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010 Mar 23;340:c332.
58. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, Lloyd A, Scalone L, Kind P, Pickard AS. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. Value Health. 2012;15(5):708–15.
59. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, Ferguson D, D'Agostino R Jr. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000;26(2):191–208.
60. Meston CM, Freihart BK, Handy AB, Kilimnik CD, Rosen RC. Scoring and Interpretation of the FSFI: What can be Learned From 20 Years of use? J Sex Med. 2020;17(1):17–25.
61. Rincón-Hernández AI, Parra-Carrillo WC, Álvarez-Muelas A, Peñuela-Trujillo C, Rosero F, Espitia de la Hoz F, González JM, Saffon P, Vélez D, Franco E, Rojas M, Vallejo-Medina P. Temporal stability and clinical validation of the Spanish version of the female sexual function inventory (FSFI). Women Health. 2021;61(2):189–198.
62. Berner MM, Kriston L, Zahnradnik HP, Härter M, Rohde A. Validation and reliability of the German Female Sexual Function Index (FSFI-d). Geburtsh Frauenheilk. 2004;64:293–303.
63. Maurer W, Hothorn L, Lehmacher W. Multiple comparisons in drug clinical trials and preclinical assays: a priori ordered hypotheses. In: Vollmar J (ed.). Biometrics in the Pharmaceutical Industry. Stuttgart: Fischer: 1995;6:3–21.
64. Morgan-Ortiz F, Contreras-Soto JO, Soto-Pineda JM, Zepeda MA, Peraza-Garay FJ. Comparison between unidirectional barbed and polyglactin 910 suture in vaginal cuff closure in patients undergoing total laparoscopic hysterectomy. Surg Technol Int. 2013Sep;23:143–8.
65. Neubauer NL, Schink PJ, Pant A, Singh D, Lurain JR, Schink JC. A comparison of 2 methods of vaginal cuff closure during robotic hysterectomy. Int J Gynaecol Obstet. 2013;120(1):99–101.
66. Nambi Gowri K, King MW. A Review of Barbed Sutures-Evolution, Applications and Clinical Significance. Bioengineering (Basel). 2023Mar 27;10(4):419.
67. Medtronic. V-LocTM Wound Closure Device Product Catalog. 2009. Available online: https://www.medtronic.com/content/dam/.
68. Ethicon Inc. STRATAFIXTM Knotless Tissue Control Device Product Catalog. 2018. Available online: https://www.jnjmedtech.
69. Corza Medical. QuillTM Barbed Suture Product Catalog. 2021. Available online: https://corza.com/wp-content/uploads/.

Publisher's Note