

Robot-assisted laparoscopic surgery versus open surgery
for radical prostatectomy

Robot-assisted laparoscopic surgery versus conventional
laparoscopic surgery for simple or radical hysterectomy



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Executive Summary

Cancer of the prostate and cancer of the female reproductive organs are common diseases and a frequent cause of cancer-related death in Switzerland. In men, radical prostatectomy (i.e. surgical removal of the prostate gland, both seminal vesicles, and a portion of both vas deferens) is a treatment option for patients with localized cancer and can be performed as an open or minimally invasive laparoscopic surgery, with or without support by a robot system. In women, removal of the uterus with or without its adnexa (i.e. radical or simple hysterectomy) is indicated for both benign and malignant conditions. Hysterectomy can be performed by an open abdominal, open vaginal, or minimally invasive laparoscopic approach. Laparoscopic interventions may be supported by a robot system, or not.

This Appraisal Report compares the effectiveness, safety, and cost-utility of the robot-assisted technique with those of the conventional techniques, i.e. open radical prostatectomy (ORP) and conventional laparoscopic hysterectomy (CLH). As of July 2018, a total of 33 robot systems existed in Swiss hospitals; all were DaVinci® robots with an approximate purchase price of CHF 1.8 million each.

In an Assessment Report (see Methods section and Supplementary Material) forming the basis of this appraisal, the evidence from randomized trials (as summarized in two Cochrane systematic reviews) was used to assess the effectiveness and safety of radical prostatectomy and simple or radical hysterectomy using robot-assisted laparoscopy. One review was updated for the purpose of this assessment in a Cochrane Targeted Update. The assessment of the two interventions was complemented by a comprehensive literature search of relevant health economic studies and a *de novo* cost analysis using estimates from Switzerland and data from the Swiss health insurer perspective. For the overall appraisal and formulation of recommendations, the Appraisal Committee then used the Evidence to Decision (EtD) framework. Stakeholder input was taken into account during the scoping and appraisal phases.

For RARP, the evidence of clinical effectiveness and harm was based on a single, randomized, controlled trial (326 participants) conducted in Australia. The differences in desirable effects (e.g. urinary tract and sexual function) between RARP and ORP were judged to be small, while the differences in undesirable effects (e.g. postoperative pain) were regarded as moderate. The overall quality of evidence was low. In the *de novo* cost analysis, patients with RARP incurred higher costs (approx. 4,000 CHF). However, reliable cost estimates for RARP in routine care from Swiss hospitals were scarce; this limited the validity of the economic analysis. The additional resource requirements for RARP as compared to ORP were considered moderate. Such additional requirements would become small if the use of RARP were centralized in fewer centers with higher caseloads for each robot system. The Appraisal Committee concluded that the evidence does not favor the current use of RARP in hospitals with low caseloads.

For robot-assisted hysterectomy (RAH), the evidence of clinical effectiveness and harm was based on six randomized trials (632 participants in total). The differences in desirable effects between RAH and conventional laparoscopic hysterectomy (CLH) were negligible, and undesirable effects were similar for the two approaches. Again, the overall quality of available evidence was low. The Appraisal Committee concluded that the available clinical evidence does not favor either RAH or CLH. In the *de novo* cost analysis, the costs per case of RAH for benign conditions exceeded those associated with CLH by approx. CHF 5,500. For malignant conditions such as cervical or ovarian cancer, the costs of RAH exceeded those of CLH by approx. CHF 4,300. These additional resource requirements were regarded as moderate, and the quality of the economic evidence was considered low. The Appraisal Committee concluded that the evidence of cost-utility favors the use of CLH for simple or radical hysterectomy.

The assessment did not include any analysis of published evidence on patient values, health equity, or acceptability of the robot-assisted technology by patients. The Appraisal Committee questioned whether the current practice of informing patients about the available treatment options is sufficient

to enable informed consent prior to the intervention. The patients' preference might depend on what information they receive about the surgical techniques. RARP is probably acceptable for many men because the alternative would be open surgery. In turn, RAH may or may not be acceptable for women; for many of them, the alternative would be CLH without the use of a robot system. Given that the technology is already in place in Switzerland and is covered by basic statutory health insurance, equitable access was not considered an issue *per se*.

The full recommendations are detailed on page 21 of this report.

Abbreviations

CHOP	Schweizerische Operationsklassifikation (Swiss classification of surgical interventions)
CI	Confidence interval
CLH	Conventional laparoscopic hysterectomy
DRG	Diagnosis-related group
EPIC	Expanded prostate cancer index composite
EtD	Evidence to Decision
FIGO	International Federation of Gynecology and Obstetrics
HTA	Health technology assessment
LOS	Length of hospital stay
MCID	Minimal clinically important difference
MD	Mean difference
ORP	Open radical prostatectomy
PICO	Population, Intervention, Comparison, Outcome
PLND	Pelvic lymph node dissection
RAH	Robot-assisted hysterectomy
RARP	Robot-assisted radical prostatectomy
RR	Relative risk
SMB	Swiss Medical Board

1. Background

Cancer of the prostate and the female reproductive organs are common diseases in Switzerland. Prostate cancer accounts for about 30% of cancers in men and is the second most common cause of cancer-related deaths among men.¹ The incidence of prostate cancer has nearly doubled over the last 20 years, probably due to improved screening. Cancer of the female reproductive organs accounts for about 10% of cancers in women and is the fourth most important cause of cancer-related deaths among women in Switzerland.²

Options for the treatment of prostate cancer range from watchful waiting and active surveillance for localized, low-risk stages of the disease to surgery, radiation, and hormonal therapy for more advanced disease. Radical prostatectomy is a treatment option for patients with localized prostate cancer with low and intermediate risk but is also an option for patients with higher risk of progression. Surgical intervention aims to remove the tumor while preserving urinary continence and erectile function as far as possible. Radical prostatectomy can be performed with retropubic or perineal access as open radical prostatectomy (ORP) or as minimally invasive surgery.³ The conventional laparoscopic technique is no longer used for radical prostatectomy in Switzerland, mostly because it is inconvenient for the surgeon. Robot-assisted radical prostatectomy (RARP) is a commonly used technique requiring a specific technical platform in the operating room with a suitable robot system.

Surgical removal of the uterus with or without adnexa (radical or simple hysterectomy) is a frequent gynecological intervention, but hysterectomy for endometrial, cervical, or ovarian cancer represents only a small share of these interventions. In malignant disease, radical hysterectomy is always indicated. There are also benign and premalignant conditions that require hysterectomy, e.g. benign neoplasms of the ovary, leiomyoma of the uterus, or carcinoma-in-situ of the cervix uteri. If the uterus and cervix are removed, the procedure is called total hysterectomy. Removal of the uterus alone is called partial hysterectomy. Hysterectomy can be performed using an open abdominal, open vaginal, or minimally invasive laparoscopic procedure. For laparoscopy, surgeons use either the conventional technique or laparoscopy assisted by a robot system. All available techniques are currently used in Switzerland; the choice depends on disease-related criteria but also preference of both patient and surgeon. In patients with benign conditions, vaginal access is often the preferred route for hysterectomy. For malignant conditions, open abdominal surgery has been the standard treatment in the past, but use of laparoscopy, with or without robot assistance, is increasing.

In 2015, robot systems for urologic or gynecologic interventions had been available from 10 manufacturers worldwide with only two manufacturers having market approval in Europe. In Switzerland, the DaVinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, California, USA) is the only system currently used for radical prostatectomy as well as for simple or radical hysterectomy. Based on information retrieved during the assessment period, it can be assumed that at least 33 DaVinci® robot systems exist in Swiss hospitals (as of July 2018). It is important to note that most, if not all, robot systems that are currently in place in Swiss hospitals are also used for other surgical interventions, and that recommendations in this Appraisal Report do not apply to these interventions by simple analogy.

2. Methods

By applying the process for health technology assessment (HTA) reports established by the Swiss Medical Board (SMB), the SMB Executive Committee decided to assess the subject of this report after broad consultation with stakeholders. Topic selection was followed by a scoping process which led to the identification and refinement of questions to be answered in the present Assessment Report. The broad subject of robot-assisted surgery was thus operationalized in two Population Intervention Comparison Outcome (PICO) questions. Guided by criteria such as frequency of disease and interventions in Switzerland, resource requirements, and balance between the sexes, the Executive Committee decided to focus on radical prostatectomy and simple or radical hysterectomy using robot-assisted laparoscopy, with both interventions being compared to the conventional surgical techniques commonly used in Switzerland.

Medical societies and other stakeholders were invited by the assessment team to comment on the PICO questions drafted for RARP, and modifications were made accordingly. The evidence of clinical effectiveness and safety of RARP had already been described in a Cochrane review published in September 2017, comparing laparoscopic and robot-assisted surgery with open surgery for the treatment of localized prostate cancer.⁴ This systematic review formed the basis of the Assessment Report, but only the comparison with ORP was used. Similarly, a Cochrane review provided the evidence of clinical effectiveness and safety of robot-assisted radical hysterectomy⁵. Since this systematic review was published in December 2014, the SMB asked Cochrane's evidence consultancy unit, Cochrane Response, for a so-called Targeted Update of this review (see Supplementary Material). The SMB refrained from a formal scoping process for this PICO question. The Targeted Update was delivered in March 2018. The choices made in the underlying Cochrane review with regard to review outcomes were re-examined and confirmed by the assessment team. This group then conducted a systematic literature search to identify relevant health economic studies. The retrieved studies were critically appraised, and *de novo* cost analyses and budget impact analyses were performed using estimates from one Swiss university hospital (see Assessment Report for detailed description of methods).

The draft of the Assessment Report was sent to the stakeholders. They were invited to comment in writing or by attending a hearing in October 2018, at which both the assessment team and members of the Appraisal Committee were present. Subsequently, the Appraisal Committee discussed the available evidence in its regular meeting while taking into account the preceding scoping document, the Assessment Report, and the feedback received from stakeholders. The appraisal employed the Evidence to Decision (EtD) framework and included the elaboration of recommendations (see Supplementary Material). The EtD framework considers several domains such as the balance between desirable and undesirable effects, quality of the evidence, resource requirements, and cost-utility, patient values, health equity, acceptability, and feasibility.⁶ The recommendations are formulated as 'strong' or 'conditional' in favor of a given intervention, in favor of either the intervention or the comparator, or against the intervention.

The present Appraisal Report was drafted from October to December 2018 and is complemented by the following documents that are available online as Supplementary Material (www.medicalboard.ch):

1. Scoping document,
2. Assessment Report (12 Sept 2018),
3. Targeted Update of Cochrane review by Liu et al. (2014),
4. Responses by stakeholders,
5. Summary of appraisal using EtD framework.

3. Results of the appraisal

Sections 3.1 and 3.2 present the results of the appraisal in the domains of clinical effectiveness and harm as well as resource requirements for the two PICO questions (i.e. radical prostatectomy and simple or radical hysterectomy using robot-assisted laparoscopy), respectively. Section 3.3 details the considerations of patient values, health equity, acceptability, and feasibility that apply to both PICO questions.

3.1 Robot-assisted radical laparoscopic prostatectomy

3.1.1 Evidence of clinical effectiveness and harm

3.1.1.2 Desirable effects

Evidence

Based on evidence from one randomized controlled trial in 326 participants, RARP likely resulted in little to no difference in urinary tract function when compared to retropubic ORP (mean difference [MD] -1.30, 95%CI -4.65 to 2.05, with minimal clinically important difference [MCID] = 6 points). Furthermore, RARP did not appear to result in any significant difference in sexual function (MD 3.90, 95%CI -1.84 to 9.64 with MCID = 10 points). RARP reduced the length of hospital stay (LOS) by one or two days (MD -1.72 days, 95% CI -2.19 to -1.25 with MCID = 1 day). In addition, RARP did not appear to be associated with any difference in the need for blood transfusions (RR 0.16, 95% CI 0.02 to 1.32).

Additional considerations

Some observational studies that were not included in the formal assessment reported that both urinary tract and sexual functions were better in men treated with RARP than in those treated with ORP. However, such data need to be interpreted with caution given the increased risk of bias in these studies. A national cohort study conducted in England included all men diagnosed with prostate cancer in England between 1st April and 31st October, 2014, who underwent prostatectomy in the National Health System.⁷ Eighteen months after diagnosis of the cancer, RARP was associated with better sexual function than ORP on the EPIC-26 sexual function scale. However, the difference between RARP and ORP was only 4 points (scale from 0 to 100) while the established threshold for a clinically meaningful difference is 10 to 12 points. This suggests that most patients would not identify this improvement in sexual function as important. There was no significant difference in other functional parameters, including continence or health-related quality of life. Another study in a cohort of patients from the Medicare database in the USA reported comparable rates of complications and the need for additional cancer therapies after RARP and ORP⁸. Although RARP was associated with a lower risk of blood transfusions and slightly shorter LOS, these benefits did not translate into decreased expenditures and were mostly due to the laparoscopic approach. The clinicians consulted for this Appraisal Report pointed out that RARP offers physical convenience to the surgeon, who can perform RARP in a more comfortable sitting position and without trembling of hands and instruments. While this might be true, it does not necessarily affect the comparison of RARP and ORP with respect to desirable effects.

Judgment

The Appraisal Committee concluded that the differences in desirable effects between RARP and ORP were small in the study included in the assessment.

3.1.1.2 Undesirable effects

Evidence

Based on the evidence from one randomized controlled trial in 326 participants, RARP appeared to result in some reduction in postoperative pain as compared to ORP after one day (MD -1.15; 95%CI -1.68 to -0.62) and after one week (MD -1.13; 95%CI -1.65 to -0.61). However, there seemed to be little or no difference in postoperative pain after 12 weeks (MD 0.01, 95%CI -0.32 to 0.34). In addition, RARP appeared to result in little to no reduction of surgical (intra- and perioperative) complications of any severity (RR 0.41, 95%CI 0.16 to 1.04) and of serious postoperative complications (RR 0.16, 95% CI 0.02 to 1.32) although the point estimates suggested that RARP may have a potential to reduce these undesirable effects.

Additional considerations

Given that RARP was only compared to ORP, any reduction in postoperative pain may be attributed to the laparoscopy itself, and it is unlikely that postoperative pain reduction is a specific effect of using the robot system. Furthermore, there might be some disadvantages with robot-assisted surgery that are not seen with conventional laparoscopy or with open surgery. For instance, patients need to be wrapped in plastic foil during the intervention, the positioning during the intervention differs, and there may be an additional need for perfusions. Additionally, conversion to open surgery might sometimes be necessary, which confers a considerable prolongation of total operating time.

Judgment

The Appraisal Committee concluded that the differences in undesirable effects between RARP and ORP were moderate.

3.1.1.3 Overall quality of the evidence

For the included outcomes, the evidence of clinical effectiveness and harm was of moderate or low quality. For one of the *critically important* outcomes (i.e. serious postoperative complications), the quality of evidence was low. Consequently, the *overall* quality of the evidence of clinical effectiveness and harm was low.

The included outcome data originated from postoperative follow-up for the first 12 weeks. However, prostate cancer survivors deal with the potential adverse effects of the surgery, such as urinary incontinence or erectile dysfunction, for years. Consequently, the available research evidence appears to be insufficient to guide clinical decision-making. The data from mid-term to long-term follow-up in the included study were published only after completion of the Assessment Report. Urinary tract and sexual function did not differ between RARP and ORP after 6, 12, and 24 months.⁹ The significant difference in cancer recurrence (RARP 3% vs. ORP 9%) was explained by the absence of standardization in postoperative management and the use of additional cancer treatments. The study authors concluded that the benefits of the robot-assisted approach are largely related to its minimally invasive nature.

When assessing newly developed surgical techniques such as robot-assisted laparoscopy, appraisal of the ongoing evolution of the procedure and technology is a challenge. Available research evidence may originate from studies that have used a first-generation device, whereas the next (and possibly improved) generation may have already been introduced outside the trial setting. This hampers a fair comparison of interventions at one particular point in time.

Furthermore, stakeholders pointed to the learning curve of surgeons performing the new technique in clinical trials and routine care. Certain outcomes of surgery depend on the surgeon's experience and the center's caseload. The design of the one trial included in this assessment did not account for differences in the performance of surgeons; RARP and ORP were performed by two different

surgeons whose experience with their respective technique (number of interventions performed) varied. Any resulting difference in patient outcome might be explained by such factors rather than by the actual surgical approach.

Presently, there are no clinical guidelines in Switzerland for the use of robot-assisted surgery in prostate cancer. The choice of surgical technique is a case-by-case decision based on local preferences, expertise, and availabilities, which also includes aspects of comorbidity.

Judgment

The overall quality of the evidence was judged as low.

3.1.1.4 Balance between desirable and undesirable effects

Based on the available evidence, there are no substantial differences between the two surgical approaches, especially in patient-relevant outcomes.

Judgment

The balance between benefits and harm was judged differently for outcomes in the short term and the long term. The Appraisal Committee deemed that the balance between desirable and undesirable effects probably favors RARP for short-term outcomes, while for long-term outcomes the balance does no longer favor RARP.

3.1.2 Considerations about resource requirements

Evidence

In the *de novo* cost analysis of radical prostatectomy, two scenarios were examined from a health insurance perspective. First, it was assumed that in any given hospital, a robot system would perform 50 RARP interventions and 25 other surgical interventions per year (base case #1). This scenario led to higher total costs per patient for RARP (CHF 24,495) compared to ORP (CHF 20,532). The cost difference between the interventions thus amounted to CHF 3,963, which was mainly driven by the higher costs of surgical equipment for RARP (excess of CHF 8,055). In contrast, estimated costs for the hospital stay after RARP were lower (by CHF 2,826) because of the shorter LOS. Costs for staff and operating room were CHF 891 less for RARP under the assumption that hourly rates for the operating room and operating surgeons were the same for both RARP and ORP. Costs due to complications in the perioperative period did barely differ (CHF 376 lower with RARP). Base case #2 assumed that 100 RARP interventions and no other robot-assisted surgeries were performed per year. In this scenario, the excess cost per RARP patient (compared to ORP patients) decreased to CHF 2,417. When the number of robot-assisted interventions was increased to 209 in our model, a threshold was reached after which the costs per patient was lower with RARP than with ORP.

A main factor that drove the cost difference between RARP and ORP in our cost analysis was the initial costs to purchase the robot system and its overall life span. If the costs for the robot system were excluded from the model, the cost difference between RARP and ORP in base case #1 decreased from CHF 3,963 to CHF 196. Additional factors were (i) hourly rate for use of the operating room for either intervention, (ii) total number of robot-assisted surgical interventions per year, and (iii) the costs for hospital stay (excluding surgery).

Additional considerations

Our *de novo* cost analysis did not take into account all costs for RARP and ORP but focused on cost items that were assumed to differ between the two interventions. During the appraisal, it was suggested that robot-assisted surgery requires more time for preparation in the operating room and that usually one or two additional staff are required. At the same time, it was argued that a robot-

assisted surgical intervention may require only one surgeon, leading to lower estimates of staff costs. However, our cost analysis was based on limited information since many of the contacted centers did not respond.

Currently, it seems difficult to obtain robust empirical data on the routine use of robot systems in RARP. According to stakeholders, Swiss hospitals are participating in the continued certification program for prostate cancer centers in Germany (www.dvpz.de). So far, no registry or other representative data collection to provide economic information has been established in Swiss hospitals.

Our cost analysis assumed that the price of a new DaVinci® robot system is about CHF 1.8 million, and that annual maintenance costs account for approximately 10% of the purchase price (i.e. CHF 180,000). Currently, only one manufacturer (Intuitive Surgical, Inc., Sunnyvale, California, USA) offers robot systems for radical prostatectomy in Switzerland. With lacking competition, this manufacturer has no incentive to lower the price. The first generation of DaVinci® robots currently used in Swiss hospitals will need to be replaced in the coming years. Apparently, a second-hand market of robot systems is emerging, and this will potentially lower the purchase price. This aspect was not considered in the present economic analyses.

Total costs of robot-assisted interventions include fix and variable costs and, thus, depend on the number of interventions per hospital. Swiss centers performing RARP differ substantially with respect to the number of interventions performed with the robot system. For hospitals with an annual caseload (for any robot-assisted intervention) of less than 25, the costs per intervention are even higher. The current German guideline for the treatment of prostate cancer recommends that a center should perform at least 50 RARP and an individual surgeon at least 25 RARP per year.³

Judgment

The Appraisal Committee concluded that the additional resource requirements for RARP (as compared to ORP) are moderate and would become smaller if the use of RARP was centralized in fewer centers.

Quality of the evidence about resource requirements

Available data on resource requirements and the resulting economic analysis were limited by several factors. It was difficult to obtain cost data from Swiss hospitals for the *de novo* cost analysis. Aggregated data for cost items such as daily rate for hospital stay, hourly rate for operating rooms, and costs for medical staff were made available by one university hospital only. It was assumed that staff costs (in particular for the surgeons) did not differ between RARP and ORP. Costs due to reusable and consumable materials needed for RARP seem to be highly variable and appear to depend, at least partly, on the surgeon's preference.

Our cost-analysis did not assess the potential influence of learning curves of the surgeons and other staff in the operating room (e.g. in terms of shorter duration of interventions or additional costs due to perioperative complications). In addition, potential benefits due to improved working conditions for the surgeons when performing RARP could not be quantified as a monetary benefit.

Our cost model was based on a 12-week follow-up after RARP in a single, randomized study in 326 patients. Consequently, any costs due to long-term effects (e.g. hospital readmission for cancer recurrence) were not considered. Other components for which no data were available included conversion to open surgery in the same patient, in-hospital medication costs (e.g. for anesthetics or antibiotics), and other costs during follow-up (e.g. outpatient visits or home-based care).

For a valid budget impact analysis, reliable estimates of the total volume of robot-assisted interventions would be needed. This figure is identified by a specific Swiss classification code of surgical interventions (Schweizerische Operationsklassifikation [CHOP]) used in Swiss hospital

statistics. However, it remained unclear whether this code is applied systematically thus providing a reliable estimate of the total number of robot-assisted operations performed. An additional assumption of the budget impact analysis was that the frequencies of RARP performed in Switzerland are evenly distributed among the Swiss hospitals.

Stakeholders emphasized that the same diagnosis-related group (DRG) lump sums apply to open surgery, laparoscopic surgery, and robot-assisted surgery. They argued that the costs for purchase and maintenance of the robot system, specific disposable surgical equipment, etc. would need to be included when DRG lump sums are determined for robot-assisted interventions. However, it was also argued that this is not warranted in the absence of evidence of the clinical benefit of this technology. Furthermore, since an increased DRG lump sum would cover the full cost and exceed variable costs, incentives would arise to increase the volume of interventions.

Taking into account the above-mentioned limitations, the Appraisal Committee concluded that the quality of evidence of resource requirements for RARP was low.

Does the cost-utility favor the intervention or the comparison?

The results of the budget impact analysis suggest that the total direct costs for patients undergoing RARP or ORP in Switzerland were CHF 56.1 million in 2015. It was estimated that RARP accounted for about 59% of interventions and 63% of costs. If the current practice were changed to a scenario in which only ORP is performed, savings of CHF 5.7 million could be achieved. In turn, a scenario assuming exclusive use of RARP would also decrease the total costs for radical prostatectomy but only by CHF 500,000. This is mainly due to a scale effect resulting from better exploitation of the robot systems in place with higher caseload and better amortization of the initial investment. As a consequence, costs per intervention would decrease. The current approach of a mixture of RARP and ORP in centers of varying sizes incurs additional costs as long as the annual caseload per robot system remains at a low to moderate level. Notably, an increased use of the robot system would impact only modestly on the overall budget because higher numbers of interventions imply a substantial reduction of per-patient costs.

Judgment

Taking into account the cost analysis with its assumptions and limitations, the Appraisal Committee concluded that the current practice of using RARP also in hospitals with small caseload does not favor its use compared to ORP. RARP would become cost-effective only if the number of hospitals using robot-assisted surgery was reduced.

3.2 Robot-assisted laparoscopic hysterectomy

3.2.1 Evidence of clinical effectiveness and harm

3.2.1.1 Desirable effects

Evidence

The evidence of clinical effectiveness and harm of robot-assisted hysterectomy (RAH) was based on six randomized, controlled trials involving a total of 632 participants. In one trial, RAH showed no difference in post-operative pain when compared to conventional laparoscopic hysterectomy (CLH). The mean difference was -2.00 (95%CI -16.08 to 12.08), but the pain scale (range) was not reported. Moreover, data covered interventions for benign conditions only.

In a single study in patients with endometrial cancer comparing RAH and CLH, no deaths in either treatment group occurred. Neither this nor any other study reported disease-free survival times. The evidence from two studies in benign conditions suggests small gains in quality of life in favor of RAH although data could not be pooled.

RAH may have reduced LOS by less than one day (MD -0.30 day, 95% CI -0.53 to -0.07; MCID = 1 day). It remained uncertain whether RAH led to a reduction of total operating time; the mean difference between RAH and CLH was 41.18 min with 95% CI ranging from -6.17 to 88.53 min. Both these estimates were from two studies in benign conditions only.

Additional considerations

Literature that was not formally included in this assessment documents potential advantages such as shorter operating times, decreased blood loss, fewer conversions to laparotomy, and shorter LOS for RAH compared to CLH in endometrial cancer. Surgeons practicing RAH argue that several steps of the surgery can be performed more easily with RAH than with CLH. This includes securing the uterine vessels and cardinal ligaments, performing accurate colpotomy, and oversewing the vaginal cuff. For endometrial cancer, uncontrolled studies describe more favorable results for RAH including better lymph node yield, reduced blood loss, lower complication rates and conversion rates, and shorter LOS, while the duration of surgery is comparable. Similarly, studies of robot-assisted laparoscopic radical hysterectomy in cervical cancer reported favorable results. Furthermore, case reports suggest that robot-assisted trachelectomy (i.e. removal of the cervix) may be an option for women seeking to preserve fertility because it allows better visualization of the vasculature and parametrial tissues.

In the treatment of ovarian cancer, robot-assisted surgery still seems to be uncommon because of the difficulty to perform extensive exploration of the abdomen. There is limited evidence suggesting that robot-assisted surgery may be suitable in selected cases of early ovarian cancer.

Judgment

The Appraisal Committee concluded that differences in desirable effects between RAH and CLH were negligible.

3.2.1.2 Undesirable effects

Evidence

Intra- and post-operative complications after RAH and CLH were comparable; relative risk (RR) associated with RAH was 0.76 (95%CI 0.38 to 1.53) in benign conditions and 1.47 (95%CI 0.79 to 2.72) in endometrial cancer. When compared to CLH, RAH may have led to a higher risk of needing blood

transfusions in benign conditions (RR 1.94; 95%CI 0.30 to 12.76) as well as in endometrial cancer (RR 2.94; 95%CI 0.62 to 13.87). None of the differences reached statistical significance.

Additional considerations

Compared with the conventional approach, RAH might require more port incisions, and this may increase procedural risks. Mortality has been considered an important outcome but follow-up in trials including patients with endometrial cancer of International Federation of Gynecology and Obstetrics (FIGO) stage < II was not sufficiently long to show any difference (prognosis is good in general). RAH may increase the risk of complications from anesthesia due to the particular positioning of the patient. It has been reported that RAH increases the risk of damage to the ureter, especially in ovarian surgery. With RAH and robot-assisted surgery in general, there is a complete lack of haptic feedback for the surgeon, and this requires additional training.

Judgment

The Appraisal Committee concluded that differences in undesirable effects between RAH and CLH were small.

3.2.1.3 Overall quality of the evidence

The quality of the evidence was moderate for the outcome 'intraoperative complications' but either low or very low for all others.

In Switzerland, only the DaVinci® robot system (several versions) is used. However, the studies considered were conducted abroad, and they may have used systems from other manufacturers. It remains unclear whether these systems are comparable. It is conceivable that differences between systems would entail differences in the profile of desirable or undesirable effects if robot-assisted surgery was to be used more widely in Switzerland. Another shortcoming is that intensity and duration of training that surgeons received prior to the beginning of the trials was not reported. The surgeons' experience with a new technique is an important factor that influences the magnitude of the desirable and undesirable effects observed.

The small number of studies included does not allow proper analysis of selective reporting (e.g. with funnel plots). Robot-assisted technology remains controversial because of the significant commercial interests. In the USA, hospitals promote the use of robot systems in gynecology without disclosing the inherent limitations and costs. For instance, hospital websites claim benefits such as reduced postoperative pain, shorter recovery time, and less blood loss with robot-assisted surgery. However, the few well-designed studies available to date provide insufficient evidence of the net benefit over the conventional laparoscopic technique. In addition, a considerable risk of bias was noted in a review of predominantly non-randomized studies of RAH versus other approaches.¹⁰

Judgment

The Appraisal Committee concluded that the overall quality of evidence was low.

3.2.1.4 Balance between desirable and undesirable effects

The low quality of evidence precluded a detailed appraisal of the balance between RAH and CLH regarding desirable and undesirable effects. Overall, this balance seems comparable for RAH and CLH. It appeared that RAH is rarely used in hysterectomies in Switzerland. Surgeons who were consulted stated that they almost exclusively perform CLH, despite the availability of a robot system at their center. This suggested that the level of experience with RAH in most Swiss hospitals is low, apart from very few centers.

Judgment

The Assessment Committee concluded that the available evidence for RAH probably does not favor either the robot-assisted or the conventional laparoscopic technique for hysterectomy.

3.2.2 Considerations about resource requirements

Evidence

In the *de novo* cost analysis for simple or radical hysterectomy, two scenarios were examined from a health insurance perspective. First, it was assumed that in a given hospital, a robot system would be used to perform 10 RAH interventions and 65 other surgical interventions for both benign and malignant conditions in one year (base case #1). This scenario led to higher total costs per patient with RAH as compared to CLH. The costs estimated were CHF 18,514 versus CHF 12,950 for benign conditions (difference of CHF 5,564) and CHF 19,975 versus CHF 15,642 for malignant conditions (difference of CHF 4,333). The cost increase was mainly due to the more expensive surgery equipment use with RAH. The difference between interventions for benign and malignant conditions was mainly due to different durations of the intervention (i.e. time in the operating room). In benign conditions, surgery time and related costs were higher for RAH than for CLH while the opposite was true in malignant conditions. Furthermore, a small difference in costs was related to complications: patients undergoing RAH for benign conditions had a lower risk of perioperative adverse events. In contrast, a higher risk of adverse events for RAH was estimated in malignant conditions. In both cases, the estimated differences did not reach statistical significance.

Second, it was assumed that 100 RAH interventions and no other robot-assisted surgeries were performed in one year (base case #2). RAH incurred higher costs than CLH even in this scenario. The costs estimated were CHF 16,954 versus CHF 12,950 for benign conditions (difference of CHF 4,004) and CHF 18,415 versus CHF 15,642 for malignant conditions (difference of CHF 2,773). These differences were less pronounced than those calculated in base case #1, especially for malignant conditions. Again, the total number of interventions per year determined the costs for surgical equipment and the cost difference between RAH and CLH.

Additional considerations

Realistic estimation of incurred costs would need to account for the number and qualification of staff needed to perform the surgical intervention. In one Swiss hospital, the surgery team for RAH currently comprises two senior surgeons, a surgeon in training, and two nurses. With increasing experience and routine, it may be possible to reduce the number of staff needed, and this would reduce the overall costs to be attributed to the intervention. In addition, the duration of surgery and time in the operating room can be reduced considerably (up to 70%) with increasing experience.

Judgment

The Appraisal Committee concluded the additional resource requirements for RAH as compared to CLH to be moderate.

Quality of the evidence about resource requirements

Many assumptions had to be made for the *de novo* cost analysis and budget impact analysis. Some of these were based on the sparse evidence from the studies included. The number of studies included for benign and malignant conditions was small, and estimates of desirable and undesirable effects were imprecise.

Several aspects that may have influenced differences in costs between RAH and CLH could not be included in the model. For example, oncological outcomes (e.g. overall survival, cancer-specific survival, or recurrence), long-term undesirable effects (e.g. urinary incontinence) and resulting

outpatient visits or hospital readmissions were not taken into account when considering resource requirements because there was no published evidence suggesting a significant difference between RAH and CLH.

Many of the additional considerations by the Appraisal Committee in connection with the DaVinci® robot system for RARP also apply to its use for RAH (see section 3.1.2 above). This includes the lack of precise cost estimates from Swiss hospitals, information about staff learning curve, or costs occurring when a center changes from using the conventional technique routinely to robot-assisted or vice versa.

Taking into account these limitations, the Appraisal Committee concluded that the quality of evidence about resource requirements for simple or radical hysterectomy was low.

Does the cost-utility favor the intervention or the comparison?

The results of the budget impact analysis suggested that the total direct costs of patients undergoing RAH or CLH in Switzerland were CHF 79.9 million in 2015. It was estimated that RAH accounted for about 4% of interventions and about 6% of costs for simple or radical hysterectomy in both benign and malignant conditions. If the current practice were changed to a scenario in which CLH is performed exclusively, this would entail savings of CHF 1.3 million. In turn, a scenario assuming exclusive use of RARP would increase the total costs for hysterectomy by CHF 4.0 million. This model takes into account economies of scale as a consequence of the improved exploitation of the robot systems in place.

In the short-term, increased use of RAH would cause additional direct costs as long as the caseload per robot remains low. The considerable costs for purchase and maintenance of the robot system as well as disposable equipment are only partially compensated by savings due to potentially shorter LOS. Increased use of the robot system for RAH would affect the overall costs only modestly because higher caseload substantially reduces per-patient costs.

Judgment

Taking into account the presented economic analysis, the Appraisal Committee concluded that the evidence of cost-utility favors the use of conventional laparoscopic surgery for both simple and radical hysterectomy.

3.3 Other considerations

3.3.1 Patient values

Evidence

A systematic search and assessment of the published research evidence of patient values with regard to robot-assisted laparoscopic prostatectomy and hysterectomy was not part of the formal assessment.

Additional considerations

Patients may perceive robot-assisted surgery as more precise and reliable because it is a new and promising technology. However, the lack of high-quality evidence for patient-relevant outcomes may not be sufficiently well addressed in conversations between health professionals and patients. Such information would be very important. For instance, concerns about potential complications may determine a patient's decision to undergo surgery.

Another consideration was whether patients have a true choice between surgical interventions when being referred to a particular center. Depending on the expertise of surgeons and technical platform,

the choice of center may determine which type of intervention will be proposed as first-line choice. Nevertheless, surgeon should inform patients about alternatives, even though these may not be offered by the particular center. In the context of this analysis, it could not be elucidated whether such information prior to obtaining the patient's consent is part of routine patient briefing. Additionally, other details (e.g. that the surgeon is not in the same room during the robot-assisted intervention) should be communicated in full. It was argued that, in the absence of any clear (contra-) indication for robot-assisted surgery, the technique might be preferred in some settings also because it will provide a training opportunity for surgeons.

Judgment

The available evidence suggests that patient perception of potential benefits or harm associated with robot-assisted surgery varies only minimally from those associated with open surgery (for prostatectomy) or conventional laparoscopic surgery (for hysterectomy). However, differences between subgroups may exist depending on patient age or presence of co-morbidities.

3.3.2 Health equity

Evidence

Systematic search and assessment of the published research evidence of health equity with a focus on access to robot-assisted surgery was not part of the formal assessment.

Additional considerations

Robot-assisted and conventional (open) prostatectomy as well as (laparoscopic) hysterectomy are available for patients with basic statutory health insurance in Switzerland. The same policy for reimbursement applies for both approaches. It is unlikely that there are subgroups in the population that would be disadvantaged systematically, e.g. by withholding the robot-assisted intervention. Patients with private health plans are more likely to be offered new technologies with unproven benefit. However, the Appraisal Committee did not attempt to corroborate this assumption with evidence specific to robot-assisted surgery. In the absence of clear clinical guidance in which cases a robot-assisted intervention is clearly indicated (or not), the choice will heavily depend on the preferences of both patients and surgeons. For instance, in one Swiss hospital, patients with endometrial cancer (FIGO stage < II) who are eligible for robot-assisted surgery are very likely to actually receive this type of intervention while this may not be the case in other centers. Given that there is little support for the superiority of one approach over the other, the question of equitable access to the new technology may be of less importance than if one option was clearly superior.

Judgment

The Appraisal Committee concluded that the choice between robot-assisted and conventional surgery for prostatectomy and hysterectomy does not impact on health equity.

3.3.3 Acceptability

Evidence

Systematic search and assessment of the published research evidence of the acceptability of robot-assisted surgery for both patients and health professionals was not part of the formal assessment.

Additional considerations

If robot-assisted technology is being promoted in the general public, a conventional approach such as open laparotomy might be perceived as an outdated technique. Patients' preference for or against

the use of a robot system during surgery might not be pre-determined *per se* but may heavily depend on what information they receive.

The Appraisal Committee discussed that, other than with drug interventions, a new technology is much more likely to enter the healthcare sector without the regulatory requirement to first demonstrate any net clinical or health economic benefit. Consequently, there are no hurdles for manufacturers to introduce such new technologies to the market. There is no strong legal instrument to regulate the use of robot systems in Swiss hospitals.

General feedback from practitioners who perform both robot-assisted and conventional surgery for either indication revealed that the robot system is associated with higher comfort for the operating surgeons and is thus more acceptable from their perspective. Robot-assisted surgery has some technical advantages such as three-dimensional vision, better and more precise visibility of the surgical site, better ergonomics, a higher degree of freedom of the robotic instruments, and a reduction of tremor interference.

On the other hand, lack of direct access to the patient has been mentioned as a disadvantage.^{11 12} Some surgeons seem to prefer open hysterectomy for malignant conditions when pelvic lymph node dissection (PLND) needs to be carried out as part of the intervention. It appears that they are more likely to achieve the intended result if PLND is performed by laparotomy. Gynecological surgeons emphasized that robot systems may be used less frequently if the expected time needed for preparation or the intervention itself is longer than with CLH, and explained that they might prefer CLH even though the robot system is available at their hospitals.

An additional aspect mentioned was that it may be of less interest for surgical trainees to learn the open surgery technique if it is perceived as outdated. Opportunities to perform it regularly may even become rare in some hospitals. The Appraisal Committee considered that in the future, a patient's risk of undesirable effects might increase if open surgery is clearly indicated but attending surgeons will be less well trained and experienced with this approach.

Judgment

The Appraisal Committee concluded that from the patients' perspective, RARP is probably favored (also because the alternative is not minimally invasive), and RAH may or may not be favored (because the alternative is minimally invasive). From the surgeons' perspective, robot-assisted technology seems to be favored only if the operating team is highly experienced thus ensuring controlled duration of the intervention.

3.3.4 Feasibility

Evidence and additional considerations

Robot systems suitable for both radical prostatectomy and simple or radical hysterectomy are in place in many secondary and tertiary hospitals in all Swiss regions. Consequently, the technology has already been introduced and can be considered feasible from a technical and organizational point of view.

Judgment

The Appraisal Committee concluded that the feasibility of robot-assisted surgery is no longer a matter of debate. This does not preclude a discussion about its economic sustainability in the long term and possibilities to optimize use the existing robot systems in the centers. In particular, caseloads that are too small to justify the initial investment and that may drive unwarranted broadening of the clinical indication should be avoided.

4. Recommendations

For radical prostatectomy, the Appraisal Committee issues a conditional recommendation for either robot-assisted laparoscopic intervention or open surgical intervention. Use of the robot-assisted laparoscopic technique should be conditional on a minimum caseload per center.

For simple or radical hysterectomy, the Appraisal Committee issues a conditional recommendation against the use of the robot-assisted laparoscopic technique.

1. Justification

There is some evidence indicating that patients undergoing radical prostatectomy may benefit from robot-assisted laparoscopy, at least in the short term after surgery. There is no evidence for a net benefit of robot-assisted hysterectomy for patients with benign or malignant conditions.

2. Subgroup considerations

For both radical prostatectomy and simple or radical hysterectomy, it is important to consider that the balance of desirable and undesirable effects between surgical approaches may depend on patient criteria such as age or comorbidity. In addition, there are differences between robot-assisted hysterectomy for benign and malignant conditions that may be important for the individual choice of surgical technique.

3. Implementation considerations

Robot-assisted laparoscopic surgery should be restricted to hospitals with a minimal number of interventions per year for quality and economic reasons. The minimal caseload for Swiss hospitals should be determined based on an in-depth analysis of relevant data from the Swiss healthcare system, and, ideally, a structured consensus process with the participation of stakeholders.

The present Appraisal Report assessed the use of robot-assisted surgery for two selected indications but not for robot-assisted surgery in general. The information provided to patients, the general public, and decision makers (e.g. in hospitals) should reflect the current state of knowledge and avoid any extrapolation to future generations of the devices.

4. Monitoring and evaluation

Hospitals incur high costs at the time of purchase of the robot system. This entails the potential that the use of robot systems is promoted with the aim of better amortization and to provide training opportunities for surgical staff. To date, there is no systematic collection of data (e.g. a registry) on the use of robot-assisted technology in the centers, either within the specialties using the technique or across specialties. Given that the number of hospitals using such robot systems is still limited, efforts should be made to improve the monitoring of this technology and to systematically collect outcome data.

5. Research priorities

In the light of the large numbers of patients undergoing robot-assisted surgery in routine healthcare, the paucity of research evidence from comparative studies is striking. Targeted clinical research should include studies of adequate size and length of follow-up that measure critically important patient-relevant outcomes. This may include investigator-initiated trials or prospective cohort studies involving multiple centers. Such studies should allow estimating with greater confidence the desirable and undesirable effects of the technology, which is crucially needed for evidence-based decision making. Methods of implementation research, such as mixed quantitative and qualitative studies, may be employed to better understand contextual factors, e.g. whether robot-assisted technology is accepted by patients and health professionals.

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