



Evolution of minimal access breast surgery

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Abstract: Surgical management of breast cancer has been evolving rapidly over the past 20–30 years. Prior to this, conventional surgical options were limited to either a mastectomy or breast conserving surgery. The demand for better aesthetic outcomes had driven the development of oncoplastic breast conserving surgery where glandular rearrangement or replacement coupled with thoughtfully placed incisions became the standard approach to breast conserving surgery. As breast surgeons and patients demand for improved aesthetic outcomes, minimally invasive or minimal access breast surgery has gained much attention over the past two decades, from endoscopic assisted to robotic-assisted breast surgery more recently. However, there has been a lack of review articles discussing this relatively recent but under-reported subset of surgical techniques in the management of breast cancer. This article aims to discuss the concept and development of minimal access breast surgery along with a review of current literature on its indications, techniques and outcome measures as well as a discussion on the strengths, limitations as well as future directions. Continued improvement in techniques and advancement of technology will definitely increase the likelihood of minimal access techniques being placed as the standard of care in the management of breast cancer.

Keywords: Minimal access; minimally invasive; robotic; endoscopic; breast surgery

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Introduction

Minimally invasive breast surgery, a term coined over the past 2 decades or so essentially described surgical techniques performed with the assistance of endoscopic instruments and more recently robotic surgical platform. Key features of this technique revolved around adequate yet small incision(s) placed in inconspicuous or hidden areas leading to better aesthetic outcomes, while not compromising on safety and allowing for immediate breast reconstruction to be performed through the same incision(s) (1-3). The use

of endoscopic instruments or robotic surgical platform help to improve visualization through better optics and thereby allowing for oncologic resection to take place through small incisions (2,4-6). Endoscopic-assisted mastectomy was first performed and popularized in a few Asian countries (1,5,7-10), where the obvious advantage seemed to be better aesthetic outcomes for women with small breasts in whom a breast conserving surgery resulted in poor aesthetic outcomes as well as the risk of inadequate resection or margin involvement. Endoscopic-assisted breast conserving surgery (E-BCS) (11-16) was also subsequently performed

with glandular rearrangement or level I oncoplastic techniques. There were multiple studies reporting on the technical feasibility, aesthetic and safety outcomes of the technique over the years but it has yet to become the mainstream or standard in the surgical management of breast cancer (1,5,7-16). Possible reason for this includes the lack of long-term follow-up data to establish oncologic safety in terms of loco-regional and distant recurrence as well as disease survival outcomes data. In addition, patient selection and suitability may be another factor on why endoscopic-assisted surgery was not routinely offered and established as standard of care (2,3). More recently, robotic-assisted breast surgery, especially robotic-assisted nipple sparing mastectomy (R-NSM) has gained attention as the possible next step in the evolution of minimally invasive breast surgery (17). So far, there have been a few case series reporting on the technical feasibility, safety and early oncologic outcomes of robotic-assisted mastectomy in a few centers worldwide (18-22). The results were promising and encouraging, however, a recent US FDA safety communication (23) seemed to be casting a doubt and raising a need for closer scrutiny as well as evaluation of this technique to ensure oncological safety are not compromised with the use of this technique in the management of breast cancer. This review article strives to discuss the concept and development of minimal access breast surgery along with a review of current literature on its indications, techniques and outcome measures as well as a discussion on the strengths, limitations as well as future directions that could possibly place minimal access breast surgery as a standard of care in the surgical management of breast cancer.

Discussion

The concept of minimally invasive versus minimal access breast surgery

The term 'minimally invasive' has been used to describe endoscopic- and robotic-assisted breast surgery as well as other surgical procedures throughout the years (24). However, the authors suggest that the term 'minimal access' be used in place of 'minimally invasive' in the context of breast surgery for two main reasons: firstly, the incision or access is smaller or hidden if compared to conventional approach; secondly, the dissection and disruption of breast parenchyma are often more extensive in endoscopic- or robotic-assisted breast conserving surgery if compared with conventional methods. The reason lies in the placement of

aesthetically pleasing incisions far from the area of interest hence resulting in more extensive dissection required for oncologic resection to take place. For example, endoscopic-assisted wide excision of a tumour in the lower inner quadrant through an axillary incision will require dissection of skin flap as well as breast parenchyma from axilla towards the lower inner quadrant whereby a conventional approach will only entail a peri-areolar incision and shorter dissection towards the tumour hence resulting in lesser tissue disruption and trauma.

Minimal access breast surgery: what it truly stands for?

In line with the concept of minimal access breast surgery, the authors suggest that there are two main broad categories of surgical techniques with or without the use of endoscopic instruments (*Figure 1*). Under non-endoscopic group, there are various techniques which can be employed and that include but not limited to moving window and retraction with light handle retractors. Endoscopic-assisted breast surgery (EABS) can be further divided into robotic-assisted and endoscopic-assisted non-robotic techniques. Endoscopic-assisted non-robotic techniques can be further subdivided according to variations in instruments used such as the use of retraction or insufflation system, single versus multiple ports, use of 3-dimensional (3D) or 4K resolution system.

History & development of endoscopic (non-robotic assisted) and robotic-assisted breast surgery

For the ease of reference to previous studies, endoscopic-assisted non-robotic breast surgery will be interchangeably used with the more familiar terms of E-BCS or endoscopic-assisted nipple sparing mastectomy (E-NSM). First case series of E-BCS and E-NSM were reported in 2001 (1) and 2002 (25) respectively, with both studies demonstrating feasibility and satisfactory aesthetic outcomes. Over the next 2 decades, there were altogether 28 studies on EABS (26) with 15 studies on E-BCS (27) and another 14 studies on E-NSM (28-34) (*Table 1*). Cohort studies comparing conventional and E-BCS or E-NSM showed comparable surgical and short or medium-term oncologic outcomes (*Tables 2,3*).

R-NSM, on the other hand was first reported in 2015 by Toesca *et al.* (35) whereby a case series of 3 patients who were BRCA mutation carriers received risk reducing mastectomy (RRM) and the authors concluded that the

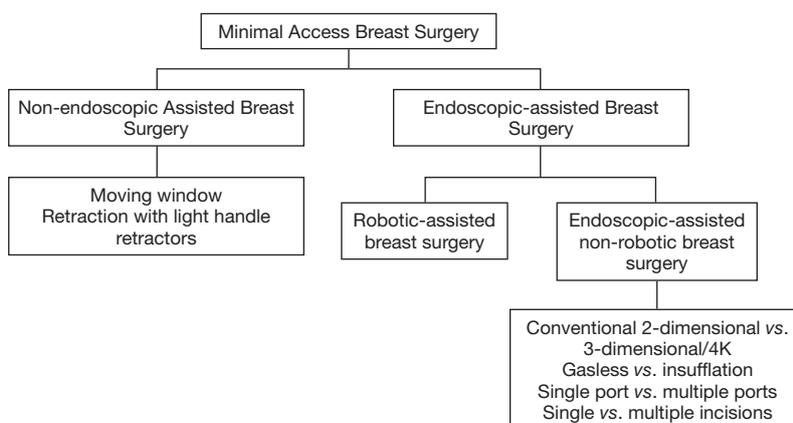


Figure 1 Flowchart of minimal access breast surgery.

Table 1 Summary of studies

Surgical techniques	Number of studies
Endoscopic-assisted breast conserving surgery alone	9
Endoscopic-assisted breast conserving surgery vs. conventional breast conserving surgery	6*
Endoscopic-assisted mastectomy alone	8
Endoscopic-assisted mastectomy vs. conventional mastectomy	4*
Endoscopic-assisted mastectomy vs. conventional breast conserving surgery	2
Total number of studies included	28

*, one study compared both E-NSM/C-NSM and E-BCS/C-BCS. E-NSM, endoscopic assisted nipple sparing mastectomy; C-NSM, conventional nipple sparing mastectomy; E-BCS, endoscopic-assisted breast conserving surgery; C-BCS, conventional breast conserving surgery.

technique resulted in a feasible and safe operation with better aesthetic outcomes. Over the course of next few years, there were altogether 4 case series (*Table 4*) reporting on respective institutional experience in the development of R-NSM (18-20,22) with authors from one of the institutions reporting on the learning curve evaluation of this technique in a separate study (21). The advantages reported in all 4 series were similar and that include better visualization with 3D optics and improved ergonomics from instruments with high degree of freedom of movement. The three main disadvantages of this technique were attributed

to prolonged operative time, increased cost as well as availability of robotic surgical platform.

Current evidence on EABS in terms of indications, techniques and outcome measures

Endoscopic-assisted non-robotic breast surgery

Indications for E-BCS mainly consisted of early breast cancer with no evidence of multiple lymph node metastasis, skin or chest wall invasion and similar for E-NSM except that no invasion of nipple areolar complex (NAC) as well as multicentric or multifocal cancer were additional indications suitable for E-NSM. Over the years, changes in techniques such as the use of insufflation in place of retraction for improved visualization and sparing of peri-areolar incision with a change towards a single axillary incision E-NSM resulting in improved surgical outcomes from reduction of NAC necrosis were just two of the many technical improvements made.

Studies conducted over the years have shown the technical feasibility of EABS in achieving equivalent surgical outcomes to conventional surgery. As discussed earlier, the increased operative time in EABS did not result in increased complications and could be reduced after overcoming initial learning curve. There was no clinically or statistically significant increase in terms of intra-operative blood loss. Common complications associated with EABS were similar to conventional techniques and include skin flap or nipple necrosis and this could be attributed to the skin flap thickness and therefore blood supply to the flap especially in cases where the dermis was exposed. Studies using tumescent for skin flap reported ease of dissection and maintenance of

Table 2 Cohort studies and selected case series on endoscopic assisted breast conserving surgery

No.	Author	Year of publication	Number of patients	Operative method	Average operation time (minutes, range or ± SD)	Intra-operative blood loss (ml or g)	Margin positive	Complications	Follow-up (months)	Local recurrence	Distant metastases	Death
1	Park <i>et al.</i> (15)	2011	40	E-BCS	BCS + SNB: 102.1±22.9; BCS + Ax: 139.5±30.3	No data	5% (2/40)	No data	12	0%	No data	No data
			681	C-BCS	BCS + SNB: 102.38±28.8; BCS + Ax: 122.49±40.5	No data	10.6% (85/681)	No data	12	0.3% (2/681)	No data	No data
2	Takemoto <i>et al.</i> (27)	2012	60	E-BCS	69 [55–104]	45 [10–80]	28.3% (17/60)	Mesh infection: 11.7% (7/60)	No data	No data	No data	No data
			51	C-BCS	93 [77–106]	100 [58–150]	25.5% (13/51)	No data	No data	No data	No data	No data
3	Ozaki <i>et al.</i> (11)	2013	73	E-BCS	BCS: 130.5±32.4; BCS + SNB: 148.1±42.7; BCS + Ax: 189.7±40.0	BCS: 51.6±35.9; BCS + Ax: 106.0±50.4	1.4% (1/73)	Partial wound necrosis: 5.4%; Partial skin flap necrosis: 2.7%; Postoperative bleeding: 1.4%	18.1 [12–30]	0%	0%	0%
4	Takahashi <i>et al.</i> (10)	2014	100	E-BCS	No data	No data	4%	No data	23 [9–40]	0%	0%	0%
			150	C-BCS	No data	No data	3.3%	No data	No data	No data	No data	No data
5	Lai <i>et al.</i> (9)	2016	46	E-BCS	193±69 [65–325]	40.2±20.2 [10–100]	6.5% (3/46)	No data	No data	0%	0%	0%

E-BCS, endoscopic-assisted breast conserving surgery; C-BCS, conventional breast conserving surgery; BCS, breast conserving surgery; SNB, sentinel lymph node biopsy; Ax, axillary lymph node dissection.

Table 3 Cohort studies and selected case series on endoscopic assisted nipple sparing mastectomy

No. Author	Year of publication	Number of patients/breasts treated	Operative method	Average operation time (minutes, range or \pm SD)	Intra-operative blood loss (mL or positive, g)	Margin n (%)	Complications, n (%)	Follow-up (months)	Local recurrence metastases	Distant recurrence metastases	Death
1 Kitamura <i>et al.</i> (28)	2002	20/21	E-NSM	237 \pm 60	356 \pm 286 g	1 (4.8)	Prosthesis related complications: 1 (4.8)	19.2 \pm 9.8 (5.8–35.2)	No data	No data	0%
2 Fan <i>et al.</i> (29)	2009	43	E-NSM	176 \pm 32	189 \pm 72 g	2 (8.0)	Prosthesis related complications: 3 (12.0) Nipple or skin flap necrosis: 5 (11.6)	No data	No data	No data	0%
3 Wang <i>et al.</i> (30)	2016	24	E-NSM	168 \pm 32	115 \pm 44	0%	Seroma: 6 (11.1) No data	20.1 \pm 11.9 12	5.9% 0.3% (2/681)	0% No data	1.9% No data
4 Wang <i>et al.</i> (31)	2017	30	E-NSM	BCS + SNB: 102.38 \pm 28.8; BCS + Ax: 122.49 \pm 40.5	No data	10.6% (85/681)	No data	27.77 \pm 20.43	No data	No data	No data
5 Du <i>et al.</i> (32)	2017	30	C-NSM	69 [55–104]	45 [10–80]	28.3% (17/60)	Mesh infection: 11.7% (7/60)	43.22 \pm 19.80	No data	No data	No data
6 Lai <i>et al.</i> (33)	2016	269	E-NSM/ E-SSM	282 \pm 161 [65–1,310]	104.5 \pm 74.9 [20–650]	1.1% (3/269)	Infection: 5 (3.18); skin edge necrosis: 11 (7.01); lymphedema: 15 (9.55)	74 [52–111]	0%	4.5%	3.2%
7 Lai <i>et al.</i> (34)	2018	50	E-NSM	244.3 \pm 82.8 [138–425]	74.5 \pm 47.7 [25–250]	0%	Infection: 8 (4.23); skin edge necrosis: 16 (8.46); lymphedema: 23 (12.16) Overall: 15.2% (48/315)	No data	3.2%	1.6%	3.2%

E-NSM, endoscopic assisted nipple sparing mastectomy; E-SSM, endoscopic assisted skin sparing mastectomy; C-NSM, conventional nipple sparing mastectomy; C-BCS, conventional breast conserving surgery; BCS, breast conserving surgery; SNB, sentinel lymph node biopsy; Ax, axillary lymph node dissection.

Table 4 Case series on robotic-assisted nipple sparing mastectomy

No	Author	Year of publication	Number of procedures	Average operation time (minutes, range or ± SD)	Conversion rate	Margin positive	Complications	Follow-up (months)	Local recurrence/ follow-up duration (months)
1	Toesca <i>et al.</i> (19)	2017	29	Initial 8.5–5 hours; in mature phase around 3 hours	6.9% (2/29)	0% (0/18)	2 (6.9%) cases small blistering in breast skin flap; 0% total NAC necrosis rate	12	No data
2	Sarfati <i>et al.</i> (18)	2018	63	Initial 200 min per breast; end of trial 85 min per breast	1.6% (1/63)	0% (0/2)	3 (4.8%) cases of implant infection; 1 (1.6%) implant loss; 0% total NAC necrosis rate	No data	No data
3	Lai <i>et al.</i> (20)	2019	29	Group 1 (case numbers 1–12): 287.3±77.4; Group 2 (case numbers 13–23): 270.7±84.8	0% (0/29)	1.4% (1/73)	2 (4.3%) blister formation; 2 (4.3%) small area skin flap ischemia/necrosis; 1 (2.2%) hematoma; 0% total NAC necrosis rate	18.1 [12–30]	0%/10.9±8.2 (3.4–20.2) months
4	Houevnaeghel <i>et al.</i> (22)	2019	27	343.75 min	3.7% (1/27)	No data	Infection: 4 (14.8); Hematoma: 3 (11.1); Skin necrosis: 1 (3.7); Implant loss: 3 (30.0); Skin blistering: 5 (18.5)	23 [9–40]	No data

NAC, nipple areolar complex.

adequate skin flap thickness. Nipple necrosis were mostly reported in cases whereby peri-areolar incision was used and studies with sparing of peri-areolar incision reported lower rate of nipple necrosis. One particular complication of concern would be the high rate of wound infection reported in two studies with the use of absorbable synthetic material or meshes as a volume replacement method in E-BCS. Even though the authors reported subsequent preventive measures such as the use of peri-operative prophylactic antibiotics and frequent changing of surgical gloves, the incidence of infection has not been completely eradicated and the use of these materials should be observed with caution.

In terms of aesthetic outcomes and patient satisfaction assessment, most patients were regarded as being satisfied with the cosmesis especially in terms of scar placement and length of skin incision. However, most of the assessments were done at about 3–6 months after operation and perhaps a repeat assessment should be performed at approximately 2–3 years after the initial operation such that remodeling of breast parenchyma would have been completed and also in cases where adjuvant radiotherapy is required. Details on each of the studies especially with regards to recurrence, conversion or complications rate had previously been reported in a recent review article (26).

Robotic-assisted breast surgery

Indications of R-NSM as reported in 4 case series were early breast cancer, tumor less than 5 cm with no evidence of skin, chest wall or NAC involvement. The 4 case series were slightly different from one another with one reporting on prophylactic R-NSM with pre-pectoral placement of implant (18), while another one with patient-reported aesthetic outcomes (20) and the latest one investigating the effects of different techniques of skin flap dissection on complications (22). Incisions used in R-NSM were mainly in the axilla or along the anterior axillary line at the NAC level with incision length ranging from 2.5–5 cm, depending on the breast or specimen size to be removed. One study (20) reported the use of methylene blue in marking the boundaries of breast parenchyma to aid in the dissection. Skin flap dissection were either performed with subcutaneous tunneling technique (20) or sharp dissection with Metzenbaum scissors (18). In terms of outcome measures, R-NSM was proven to be feasible and safe in all studies with low conversion rate, reasonable learning curve (21) and low complications rate. Of notable mention was the 0% NAC necrosis rate across all studies (18-20,22)

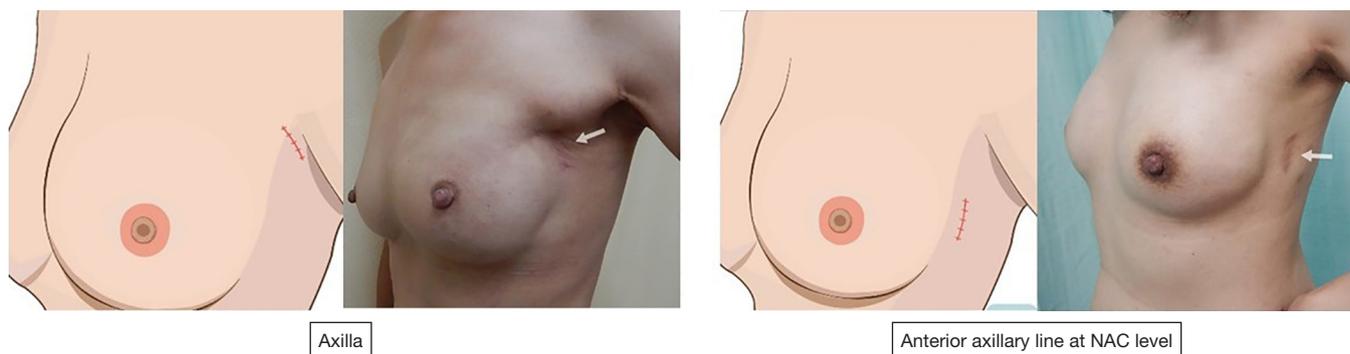


Figure 2 Common incisions used in endoscopic- and robotic-assisted nipple sparing mastectomy.

in which the authors of one study (20) attributed the low NAC necrosis rate to placement of incision far from the NAC and better visualization with 3D optics on a robotic surgical platform. Oncologic outcomes were not reported as the follow-up duration was relatively short in all studies. Excellent aesthetic outcomes were reported in all studies and in addition, one study described patient-reported satisfaction rate in which majority of patients were satisfied with the operation especially with regards to placement and length of incision (20).

Advantages and disadvantages of EABS

Endoscopic-assisted non-robotic breast surgery

E-BCS or E-NSM allows for better incision or scar placement in inconspicuous areas thereby leading to better cosmesis. Secondly, it allows for tumour resection with adequate margins and hence no compromise on short- and medium-term oncological outcomes. Thirdly, it offers better visualization with the aid of light handle retractors and allows for better precision when it comes to wide excision.

On the other hand, it has its inherent disadvantages as more equipment is required with additional time in the set-up and conduct of the operation. This leads to increased operative time if compared to conventional surgery. However, cohort studies have shown that the operative time could be reduced after overcoming initial learning curve and there was no increased risks of complications and adverse outcomes as a result of the longer operative time. Increased cost is also another possible disadvantage as there are disposable instruments used in the conduct of the operation compared to conventional surgery. The solution to this may be the use of re-usable equipment but it would be of great

value to have a cost-effectiveness analysis looking at the average cost of E-BCS or E-NSM in the long run.

Robotic-assisted breast surgery

Robotic surgical platform offered many advantages including better visualization with 3D optics, improved ergonomics from instruments equipped with a high degree of freedom of movement and better working space due to insufflation used. However, in the authors' experience, robotic surgical platform is most suitable in R-NSM compared to other types of breast surgery. As the incision was placed in the axilla or along the anterior axillary line, aesthetic outcomes were also better if compared to conventional methods (*Figure 2*). The three main disadvantages of this technique were attributed to prolonged operative time, increased cost as well as availability of robotic surgical platform.

The future and latest advancements in minimal access breast surgery

The future of minimal access breast surgery is limitless. As shown in *Figure 1*, variation of techniques can be applied in the conduct of minimal access surgery. Technique that will remain competitive and potentially develop into a standard approach should fulfill 4 criteria in terms of safety (surgical and oncological safety), efficacy, acceptable operative time and cost-effectiveness. Endoscopic-assisted surgery, be it robotic or non-robotic approach has equal chance to develop into standard approach for the surgical management of breast cancer.

Endoscopic-assisted non-robotic breast surgery

The latest advancements and improvements in non-robotic endoscopic breast surgery would be the use of insufflation as

well as 3D or 4K endoscopic system. The use of insufflation has been reported to result in better working space as well as improved hemostasis possibly due to positive pressure from the insufflation (34). The preliminary experience of the use of single port insufflation 3D endoscopic system in E-NSM was just recently reported as a new technique (36) and the authors demonstrated safety, feasibility as well as excellent aesthetic outcomes. Other than 3D system, there are also 4K high definition (HD) system in the market which could potentially improve visualization further and be used in E-NSM with insufflation.

Robotic-assisted breast surgery

Da Vinci robotic surgical platform is at the forefront of R-NSM. Da Vinci Si and Xi system were used in current reported series. New robotic surgical platform, da Vinci SP or single port system is the latest addition to the da Vinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA). In what was described as the first platform with fully wristed and elbowed instruments within a single port system through a 2.5 cm cannula, better versatility and thereby reach would be very much anticipated. However, the size of the cannula at 2.5 cm might pose significant challenge as incision may need to be extended at the end of operation for specimen extraction and this may render the small cannula size irrelevant. As the system is currently available in only selected countries or institutions worldwide, the authors would foresee increased use of the system in R-NSM in years to come. In addition, there are other robotic surgical platforms in the market offering different niche areas of expertise and the potential of their use in breast surgery are limitless (37).

International endoscopic and robotic breast surgery symposium (IERBS) 2019

In the recently concluded IERBS from 24th to 25th May 2019 in Taiwan, pioneers and experts in the field of endoscopic and robotic breast surgery came together and shared their respective institutional experience in the first conference dedicated to endoscopic and robotic-assisted breast surgery. Sharing of experience and technical know-how are of utmost importance in promoting the development of endoscopic breast surgery. In addition, experts in the field of R-NSM also came together and developed the first IERBS consensus statement on robotic mastectomy which covered 6 domains including indications, contraindications, technical considerations, patient counselling, outcome

measures as well as training and learning curve assessment. The consensus statement will be published in the near future, providing experts' opinion and guidance in the fast-developing field of robotic-assisted breast surgery.

Conclusions

The era of minimal access breast surgery is already here and will most likely stay for the next decade or so. Continued improvement in techniques and advancement of technology will definitely increase the likelihood of minimal access techniques being placed as the standard of care in the management of breast cancer. Future directions in terms of international multicenter collaborations and a structured training system for endoscopic and/or robotic-assisted breast surgery are of paramount importance while the long-term oncologic outcomes as well as cost-effectiveness analyses are much anticipated in the near future to further consolidate the use of EABS in the surgical management of breast cancer.

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Footnote

Conflicts of Interest: Dr. HW Lai was the organizing chair and founder of IERBS 2019. Dr. CW Mok was the secretary general of IERBS 2019.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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