Review Article

Role of MIS in Common Malignancies at a Glance - A Concise Review

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Abstract

The above statement by Albert Einstein very aptly answers the question if minimally invasive surgery in surgical oncology is acceptable. Yes, it is time the surgical oncologists get over their prejudices against MIS and add it as an armamentarium against cancer, given the recent evidence that MIS is at least as good as open procedures in certain cancers, at least in the early stages. MIS has already proven to be effective in a variety of non-malignant diseases. Rather it is in fact better than the open surgeries, given the advantage related to a small scar and consequent better post-operative inflammatory response. MIS in surgical oncology is an attempt to combine the advantages of MIS while retaining the radicality of surgical procedures in oncology.

MIS includes laparoscopy, robotic surgery, NOTES (Natural orifices transluminal endoscopic surgery) and thoracoscopy. MIS is now utilized in a variety of surgical fields in a multitude of surgeries and is being increasingly used in malignancies. A lot of retrospective analyses and a few RCTs have confirmed the safety and efficacy of MIS procedures and RCTs confirm non inferiority over the open ones. Although, there are occasional trials that have failed to show an equivalence. A number of RCTs are going on in various fields and results are awaited. MIS has been now accepted as a modality in various malignant GI, thoracic, urologic and gynecological procedures. Studies are going on to evaluate the utility in breast and head and neck cancers too.

We did an extensive literature search in electronic databases like Cochrane Library, PubMed, Embase and electronic search engines like Google Scholar. Keywords for each organ was used along with related terms like laparoscopy, robotic, MIS or MAS (Minimal Access Surgery). The search terms were identified in the title, abstract or medical subject heading (MeSH). Only high quality articles relevant to our research was chosen.

Keywords: Laproscopy; Tumors; Lymphoma; Trials

Staging Laparoscopy

Laparoscopy can be done alone as a staging procedure, for diagnosis and resectibility. It can also be used in combination with USG and cytology for staging and consequently better treatment decisions. GI cancers have the most utilization of laparoscopy for the purpose of pre op evaluation of the disease, staging and thereby resectibility.

SAGES (Society of American Gastrointestinal and Endoscopic Surgeons) recommends staging laparoscopy in cancers of the esophagus, stomach, pancreas and periampullary region, liver, biliary tract, colorectum and lymphoma.

Esophagus and GE Junction Tumours

NCCN states that laparoscopy may be useful in select patients in detecting radiographically occult metastatic disease, especially in patients with Siewert II and III tumours (cat 2A). They also state that laparoscopy is optional in stage I-III adenocarcinoma at GE junction. Although there are no RCTs to show a definite benefit with laparoscopy, several retrospective showed a change of treatment decisions and avoided unnecessary laparotomies in a significant number of patients [1,2].

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SAGES: Staging laparoscopy should be used for patients with esophageal cancer who are potential candidates for curative surgical resection based on a negative preoperative staging for lymph node or distant metastases. Furthermore, the procedure can be used for the placement of enteral feeding access in patients when a percutaneous endoscopic gastrostomy cannot be undertaken, and the patients are candidates for neoadjuvant chemotherapy.

ESMO: In locally advanced (T3/T4) adenocarcinomas of the Oesophago-Gastric Junction (OGJ) infiltrating the anatomic cardia, laparoscopy can be done to rule out peritoneal metastases, which are found in ~15% of patients

ICMR recommends both staging laparotomy and thoracoscopy for esophageal cancers.

Stomach

NCCN recommends staging laparoscopy from T1b tumours or higher, given that it is not metastatic. Laparoscopy can be used alone (cat 2A) or along with cytology (cat 2B). Various other societies have also given their own guidelines for staging laparoscopy. They vary as below,

SAGES-T3/T4 GC without evidence of lymph node or distant metastasis on pre op imaging.

ESMO [3] - All patients with resectable gastric cancer.

JGCA - Patients with clinical stage II-III prior to neoadjuvant treatment.

ICMR - Indications for staging laparoscopy 42-48

1. T3/T4 tumours as assessed by CT, with or without lymph

node metastases-prior to the commencement of NACT to determine treatment intent (Level 3).

2. Receipt of neoadjuvant therapy-prior to or at the time of surgical exploration for definitive resection (Level 3).

Various other retrospective and prospective studies have reinforced the utility of staging laparoscopy over the years. [4.5].

Pancreas

The NCCN guidelines recommend staging laparoscopy in all resectable high risk and borderline resectable tumours, as evidenced by pre op imaging. In borderline cases, if neoadjuvant therapy was administered and the patient didn't undergo staging laparoscopy prior to therapy, then it is recommended prior to undergoing the surgery. Intraop USG can be used as an adjunct. High risk cases in ca pancreas are defined as imaging findings casting doubts on resectability, very highly elevated CA 19.9 levels, large primary tumours, large regional lymph nodes, excessive weight loss and extreme pain.

Other society guidelines are as follows.

SAGES guidelines - Indications for staging laparoscopy.

1. As a staging procedure for pancreatic adenocarcinoma except known metastatic disease.

2. For detection of imaging occult metastatic disease or unsuspected locally advanced disease in patients with resectable disease based on preoperative imaging prior to laparotomy.

3. For assessment prior to administration of neo-adjuvant chemoradiation.

4. For selection of palliative treatments in patients with locally advanced disease without evidence of metastatic disease on preoperative imaging.

Clinical Practice Guidelines for Pancreatic Cancer 2016 From the Japan Pancreas Society proposes performing a laparoscpic examination in the case where the diagnosis of resectable pancreatic cancer or locally advanced pancreatic cancer was made but distant metastasis cannot be denied.

Consensus guidelines on pancreatic cancer Spain say that in patients with large tumours, particularly of the tail of the pancreas, borderline resection and high tumour marker, a diagnostic laparoscopy should be considered prior to laparotomy. Even after neoadjuvant therapy, those patients with suspected disease progression by either elevated Ca 19.9 without radiological evidence of disease progression should be carefully evaluated and PET CT and laparoscopy should be considered.

ICMR guidelines list laparoscopy ± biopsy as an optional procedure. Laparoscopy ± biopsy/Peritoneal washings can be done in borderline resectable, locally advanced large tumor, tumor with suspected metastatic nodes, high CA 19-9 (in absence of obstructive jaundice). It can also be done in cases where repeated EUS guided FNAC's are -ve in borderline or locally advanced or metastatic cases for planning non surgical treatment. The guidelines also state that in patients with no evidence of disease progression after neo-adjuvant therapy must be considered for laparotomy with intent to resect the tumour, thereby precluding the role of laparoscopy in resectable cases.

Those guidelines are based on several retrospective and prospective studies that enforce the efficacy of staging lapaprotomy on change on treatment following the procedure.

Biliary Tract Cancers

Gallbladder

NCCN recommends staging laparoscopy for,

- T1b or greater tumours.

- T1a tumours, in incidental ca GB if the cystic duct node is positive with or with margin positive resection.

- GB mass is detected on imaging ± jaundice.

- Suspicion of metastatic disease on imaging not amenable to percutaneous imaging.

SAGES: Recommends staging laparoscopy in known or suspected gallbladder cancer without evidence of unresectable or metastatic disease.

ICMR states that staging laparoscopy should be done in patients with suspected, resectable or advanced GBC or incidental GBC before re-exploration to rule out distant metastases. Higher yield is likely in patients with T3 and above GBC, poorly differentiated tumors and those with margin positive cholecystectomy. It may also be indicated in patients with suspicious metastasis that cannot be biopsied percutaneously.

Cholangiocarcinoma

NCCN recommends staging laparoscopy in any resectable tumour.

SAGES: Stage T2 or T3 hilar cholangiocarcinoma without evidence of unresectable or metastatic disease determined by preoperative imaging.

Although most of the other society guidelines like the Japanese Society of HPB cancers and ICMR don't mention staging laparoscopy for these tumours, several studies and meta analyses have found utility of this procedure prior to definitive surgery [6,7].

Colon or rectal cancer

Most of the guidelines including NCCN and ICMR doesn't recommend staging laparoscopy for colorectal cancer. SAGES however, is of the view that patients who have liver metastases from a primary colorectal cancer may be candidates for curative resection when there is no other extrahepatic disease, and when all of the disease in the liver is resectable. Thus, SL for these patients can provide more accurate identification of all hepatic lesions, including size, number, and location, than non-invasive imaging.

Lymphoma

SAGES: Hodgkin's lymphoma originates in one nodal group and spreads in a stepwise manner to contiguous nodal groups. Staging laparoscopy may be useful in determining the stage and location of the disease, as this may affect decisions regarding treatment, particularly the administration of chemotherapy.

In contrast, for non-Hodgkin lymphoma, the exact extent of the disease has less impact on the treatment course, and therefore, SL in non-Hodgkin lymphoma is less frequently performed. The primary indication for SL in non-Hodgkin lymphoma is for tissue diagnosis through biopsy of intra-abdominal lymph nodes in the absence of peripheral lymphadenopathy.

Laparoscopic and Robotic Surgeries

Esophagus and GE junction

NCCN guidelines state that Minimally Invasive Surgery (MIS) is acceptable for surgeries for cancer of the esophagus and GE junction. The MIS surgeries are,

1. MIS Ivor Lewis esophago-gastrectomy (laparoscopy + limited right thoracotomy).

2. MIS McKeown esophago-gastrectomy (right thorascopy + limited laparotomy/laparoscopy + cervical anastomosis.

3. Robotic minimally invasive esophago-gastrectomy.

NCCN also states that open surgery is preferred over MIS if optimal surgery with MIS approaches looks challenging.

Japanese guidelines endorse use of laparoscopy and thoracoscopy as an approach to resection of ca esophagus. ICMR guidelines doesn't mention MIS as an armamentarium for ca esophagus.

One of the first high quality RCTs was first published in the Lancet in 2012. The findings of this trial provided evidence for the short-term benefits of minimally invasive oesophagectomy for patients with resectable oesophageal cancer [8].

TIME trial [9] - The study depicted no differences in disease-free and overall 3-year survival for open and MI esophagectomy. These results, together with short-term results, further support the use of minimally invasive surgical techniques in the treatment of esophageal cancer.

A lot of studies-retrospective, prospective and RCTs have endorsed the role of MIS in ca esophagus. It has been shown that it is safe and feasible, with perioperative mortality of around 2% in upfront cases [8], although mortality rates are somewhat slightly higher post neoadjuvant therapy [10]. In a RCT of 115 patients comprising of esophageal and EGJ cancers, patient receiving MIE (Minimally Invasive Esophagectomy) had significantly lower rates of pulmonary infection than open esophagectomy. In another recent RCT of >200 patients with cancer of middle or lower 1/3 of the esophagus, a hybrid approach of laparoscopic gastric mobilisation with open right thoracotomy resulted in fewer post op complications, especially pulmonary and similar 3 yr survival as open surgery [11].

A recently published case series of 6 patients from Japan concluded that robot-assisted mediastinoscopic esophagectomy was technically feasible and safe. Use of da Vinci Surgical System may help attenuate technical difficulties in transcervical middle mediastinal lymph node dissection [12].

Stomach

Treatment of ca stomach is one of the fields where MIS has been extensively used. Laparoscopic gastrectomy was first done in 1994 in Japan. JLSSG (Japanese Laparoscopic Surgery Study Group) Meta analysis [13] on 1294 patients from the period 1994-2003 showed Mortality - 0%, Morbidity - 14.8%, Rec rate -6%. OS at 5 yr was

- Stage IA: 99.8%
- Stage IB: 98.7%
- Stage II: 85.7%

Another retrospective study-Long-term Outcomes of Laparoscopic Versus Open Surgery for Clinical Stage I Gastric Cancer - The LOC-

1 Study compared 3630 patients with EGC (Early Gastric Cancer) - LG (Laparoscopic Gastrectomy) *vs.* OG (Open Gastrectomy) from the period 2006-2012 [14]. It showed a 5 yr survival of 97.1% for LG *vs.* 96.3% for OG. The 3 yr recurrence free survival was 97.7 *vs.* 97.4 and recurrence rate 2.3 *vs.* 2.4 for laparoscopic *vs.* open gastrectomies respectively. The Korean surgeons also took up a meta analysis which showed similar results.

Since the safety and efficacy was ascertained by the above meta analyses a lot of RCTs have been taken up to answer various research questions regarding utility of MIS in various clinical scenarios. The Korean Laparoendoscopic Gastrointestinal Surgery Study Group (KLASS) has since then taken up 9 clinical trials. The Chinese Laparoscopic Gastrointestinal Surgery Study Group (CLASS) has also taken up trials in the lines of KLASS group, 2 RCTs in Japan and another 2 RCTs are going on for Ca stomach in Holland also.

KLASS group of trials

KLASS 01 [15] - The objective of the trial was todetermine the safety of laparoscopy-assisted distal gastrectomy (LADG) compared with Open Distal Gastrectomy (ODG) in patients with clinical stage I gastric cancer in Korea. It was a Phase 3, multicenter, open label, prospective RCT conducted at 13 university hospitals. They had a strict criteria for the surgeons to participate in the study - The surgeons participating in the trial were to have completed at least 50 cases each of LADG and open gastrectomy, with each surgeon's institution having a case load of atleast 80/yr. Both ITT and per protocol analysis was done since there a lot of crossover in both the groups. The morbidity rate was 19.9% in the open group *vs.* 13% in the laparoscopic group. The trial concluded that LADG is surgically safe for the treatment of stage I gastric cancer and has benefits with regard to minimising wound complications. Recently the long term outcomes of the KLASS 01 trial have been published and it shows similar OS in the laparoscopic and the open group - 94.2% *vs.* 93.3%.

KLASS 02 [16] - This trial aims to compare outcomes between Laparoscopic Distal Gastrectomy (LDG) *vs.* Open Distal Gastrectomy (ODG) for T2-T4a Ca stomach. The accrual has been completed but the results have not been published yet.

KLASS 03 [17] - It was a phase II trial whose objective was to ascertain the safety and feasibility of Laparoscopic Total Gastrectomy (LTG). It concluded that laparoscopic total gastrectomy is safe and feasible for proximal stage I gastric cancer.

KLASS 04 - This trial is ongoing for comparison oflaparoscopic pylorus preserving gastrectomy (PPG) *vs.* laparoscopic distal gastrectomy for middle 1/3 Early Gastric Cancer (EGC).

KLASS 05 - This trial ongoing for comparison of laparoscopic proximal gastrectomy *vs.* laparoscopic total gastrectomy for upper 1/3 EGC.

KLASS 06 - This trial ongoing for comparison oflaparoscopic total D2 gastrectomy *vs.* open D2 gastrectomy

KLASS 07 - This trial is ongoing for assessment of QOL of lap assisted distal gastrectomy *vs.* totally lap DG.

ROBOT trial - This is a phase II trial for comparison of morbidity and mortality for Robotic Gastrectomy (RG) *vs.* Laparosopic Gastrectomy (LG) of cT1 - cT3 tumours.

SENORITA trial [18] - This is a phase III trial to verify whether

laparoscopic stomach preserving surgery with Sentinel Basin Dissection (SBD) achieves similar oncologic outcomes and improved quality of life compared to a standard gastrectomy in EGC patients.

CLASS trials

CLASS 01[19] - It is a randomized controlled trial comparing morbidity and mortality of laparoscopic versus open D2 distal gastrectomy for advanced gastric cancer. Like the Korean trials, here also the participant surgeons had to be eligible for the study. Only those surgeons who have done at least 50 distal gastrectomies with D2 lymphadenectomy using open and laparoscopic approaches in institutions where 300 gastrectomies for patients with AGC annually are done were eligible for participation in the trial. There was no difference between the groups on intraoperative complications, post op morbidity and mortality. The lap to open conversion rate was only 4.5%.

CLASS 02 [20] - This trial is similar to the KLASS 03 trial. The results have not been published yet.

CLASS 04 trial aims to evaluate the feasibility and safety of laparoscopic spleen preserving station no. 10 lymph node dissection.

Other Chinese RCTs on ca stomach are also ongoing.

Japanese trials

They are taken by two groups in Japan - The JLSSG (Japanese Laparoscopic Surgery Study Group) and JCOG (Japanese Clinical Oncology Group).

JCOG 0703 [21] - It is a prospective phase II study to confirm the non inferiority of LADG compared with open gastrectomy in terms of OS. It concluded that long term outcome for LADG for stage I gastric cancer seems comparable to open procedures.

JCOG 0912 [22] - It is similar to KLASS 01. The results have not been published yet.

JCOG 1401 [23] - It is similar to KLASS 03 or CLASS 02 trials. The only difference being it is a non randomized trial but seeking an answer to the same research questions as the above mentioned trials. The results have not been published yet.

In Japan, a single-institution phase III trial opened in April 2018 that randomizes patients with resectable gastric cancer to either laparoscopic or robotic gastrectomy [24].

Holland: 2 RCTs are ongoing in the field of laparoscopic gastrectomy.

LOGICA trial [25] - This ongoing trial aims to compare the outcomes of laparoscopic *vs.* open gastrectomy for gastric cancer.

Stomach trial [26] - Aim of this ongoing prospective randomised, multi-center trial is to compare open gastrectomy with minimally invasive gastrectomy for gastric cancer in patients that received neoadjuvant therapy.

Currently, the JGCA(Japanese Gastric Cancer Association) guidelines only recommends laparoscopic distal gastrectomy as an optional treatment for clinical stage I cancer by experienced and in house certified surgeons which was supported by JCOG 0703, JCOG 0912 and KLASS 01 trials. They also state that laparoscopic total gastrectomy might be associated with an increased risk of post op complications during the first year of performance. This statement was given prior to the publication of results of the KLASS 03 trial, so they have termed this procedure as investigational.

On the lines of JGCA, the KGCA (Korean Gastric Cancer Association) also says that laparoscopic surgery is acceptable for early gastric cancer. But these guidelines too were laid before the results of KLASS 01, KLASS 02 and KLASS 03 trials were available.

ESMO guidelines state thatas techniques predicting lymph node involvement develop, those with negative nodes should be operated laparoscopically, whereas those with predicted positive nodes would require open surgery.

SAGES state that Open gastrectomy with a minimal lymph node dissection of 15 for staging purposes remains an appropriate surgical treatment for gastric adenocarcinoma in the west. Given the benefits of MIS, they state that are encouraged to expand indications for this approach.

ICMR has no mention of MIS procedures for Ca stomach.

Pancreas

MIS has not been extensively utilised for ca pancreas as for ca stomach. Laparoscopic Pancreatoduodenectomy (LPD) was described first by Gagner et al. [27] over 20 years ago, but since then has not gained widespread use. Laparoscopic distal pancreatectomy has gained wide acceptance. However, in the recent years, even laparoscopic pancreaticoduodenectomy has gained ground.

Several studies non randomized studies have attempted to compare the operative and oncologic characteristics of open and laparoscopic pancreatic head resection. Like in most MIS procedures, the time taken for the surgery was significantly prolonged compared to open procedures but intra op blood loss and duration of stay was significantly. Conversion to open surgery ranged from 9% to 30%. The number of lymph nodes harvested has been reported to be similar or even significantly higher in LPD compared to PD. Comparisons of R0 resection rates showed that results between open and LPD did not differ significantly.

In comparison to pancreatico-duodenectomy, there are only a few studies on laparoscopic total pancreatectomy. They show only that it was feasible and safe with apparently satisfactory oncologic outcome.

A large meta analysis of 29 studies showed superiority of laparoscopic distal pancreatectomy in terms of blood loss, time to first oral intake, and hospital stay. All other parameters of operative morbidity and safety showed no difference. Data on oncologic radicality and effectiveness were limited [28].

A recently concluded prospective observational study comparing Minimally Invasive Distal Pancreatectomy (MIDP) - Laparoscopic or Robot assisted *vs.* Open Distal Pancreatectomy (ODP) for Pancreatic Ductal Adenocarcinoma (PDAC) - DIPLOMA study, showed comparable survival after MIDP and ODP for PDAC, but opposing differences in R0 resection favouring MIDP *vs.* ODP (67% *vs.* 58%), but other parameters were in favour of the open group - resection of Gerota's fascia (31% *vs.* 60%) and lymp node retrieval (14 *vs.* 22) for MIDP *vs.* ODP. The results strengthen the need for an RCT to confirm oncological safety of MIDP [29].

Parenchyma sparing resections: Indications for parenchyma sparing approaches include mainly neuroendocrine neoplasms; serous cystadenoma and branch duct IPMN as well as solitary renal cell carcinoma metastasis. The size should not be more than 3 cm to 4 cm. Although EN does not include a reconstructive phase, the procedure is associated with a high risk for POPF (Postoperative Pancreatic Fistula). In a systematic review, it was 36.7%.

Robotic assisted surgery: The first robotic-assisted pancreatic resections were reported in 2003 by Melvin et al. [30] for distal pancreatectomy and by Giulianotti et al. [31] for pancreaticoduodenectomy. Since then, several studies have shown promising results, comparable to and at times better (conversion rate, DOS) than standard laparoscopy and open procedures. On the down side, robotic procedures have a significant learning curve.

Long term results of 130 patients of laparoscopic pancreatico-duodenectomy for pancreatic and periampullary cancer from a tertiary care hospital in South India showed an overall 5 yr actuarial survival of 29.42% and median survival of 33 months. Only one conversion to open procedure was done in the entire cohort. The mean operating time was 310 ± 34 mins. It was concluded that randomised controlled trials are needed to establish the advantages of LPD [32].

An RCT was taken up in the same hospital as the above prospective study with 64 patients, 32 in each group - Pancreatic head and periampullary cancer laparoscopic *vs.* open surgical treatment trial. The results showed median duration of postoperative hospital stay was longer for open pancreaticoduodenectomy than for laparoscopy - 13 (6-30) versus 7 (5-52) days respectively; P=0.001. Duration of operation was longer in the laparoscopy group. Blood loss was significantly greater in the open group (mean 401 ml *vs.* 250 ml; P<0.001). Number of nodes retrieved and R0 rate were similar in the two groups. There was no difference between the open and laparoscopic groups in delayed gastric emptying (7 of 32 versus 5 of 32), pancreatic fistula (6 of 32 versus 5 of 32) or postpancreatectomy haemorrhage (4 of 32 versus 3 of 32). Overall complications (defined according to the Clavien-Dindo classification) were similar (10 of 32 versus 8 of 32). There was one death in each group. They concluded that Laparoscopy offered a shorter hospital stay than open pancreatoduodenectomy in this randomised trial [33].

Another RCT - Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2) has been published recently [34]. In the study, although not statistically significant, laparoscopic pancreatoduodenectomy was associated with more complication-related deaths than was open pancreatoduodenectomy, and there was no difference between groups in time to functional recovery. These safety concerns were unexpected and worrisome, especially in the setting of trained surgeons working in centres performing 20 or more pancreatoduodenectomies annually. Experience, learning curve, and annual volume might have influenced the outcomes; future research should focus on these issues. This trial dampens the enthusiasm for MIS for pancreaticduodenectomy offered by the previous RCT.

NCCN guidelines mention that there is an increasing role for laparoscopic distal pancreatectomy. They have quoted 2 Meta analyses and one prospective study in support of laparoscopic resection. It is also mentioned that MIS pancreaticoduodenectomy is a viable option. In unresectable cases, NCCN has endorsed laproscopic gastrojejunostomy ± FJ insertion, based on 2 RCTs that showed that 20% patients had GOO who didn't undergo prophylactic gastro jejunostomy. Laparoscopic celiac plexus block can also be used.

ICMR states that laparoscopic resections for pancreatic tumours are feasible. However, they also state that at present there is no high-level evidence to suggest that laparoscopic PD is equal or superior to open surgery in terms of overall survival. Laparoscopic distal pancreatectomy has also been demonstrated to be technically feasible

with acceptable perioperative outcomes. In contrast to NCCN guidelines, ICMR states that palliative surgeries are associated not only with increased morbidity but no difference in survival compared to aborted laparotomies. Recommendation - The role of laparoscopic/robotic resections as well as synchronous vascular resections needs to be clarified.

Japanese guidelines on pancreatic cancer do not recommend performing laparoscopic pancreatectomy other than clinical trials. The utility of laparoscopic distal pancreatectomy for the treatment of pancreatic cancer has been approved by health insurance in Japan, but the significance and safety should be examined by further accumulation of cases.

Colorectal Cancer

Jacobs reported the first case of technical feasibility of laparoscopic colectomy in 1991. Technical approaches range from intracorporeal procedure, where no additional incisions are required, to extracorporeal, hand assisted, laparoscopic-assisted techniques or SILS (Single Incision Laparoscopic Surgery). For rectal cancers in addition to laparoscopic and robotic surgery, newer procedures like TEM (Transanal Endoscopic Microsurgery)/TAMIS (Transanal Minimally Invasive Surgery) and TaTME has garnered much interest in the recent years.

As with minimally invasive surgery in the other organs, laparoscopic surgery has gained a strong foothold for colon and rectal cancers. In addition to the benefits associated with MIS, mimimally invasive techniques, especially robotic surgery has the benefit of reaching upto areas inaccessible to conventional open surgery. This enhanced visualization of the pelvic structures and accessibility aids in nerve sparing procedures and going in the correct plane with minimal blood loss and lesser complications. Furthermore, the advent of TaTME has also addressed the need for better visualization at the pelvis by combination of endoscopic and laparoscopic techniques.

Barcelona trial, published in 2002, was one of the first trials to directly compare the outcomes between laparosopic and open colectomy for carcinoma of the colon. 219 patients took part in the study (111 LAC group, 108 OC group). Patients in the LAC group recovered faster than those in the OC group. Although laparoscopic group fared better for the short term outcomes, LAC did not influence perioperative mortality. Probability of cancer-related survival was higher in the LAC group (p=0.02). This superiority of LAC was due to differences in patients with stage III tumours (p=0.04, p=0.02, and p=0.006, respectively). In 2008, the long term results were published and the results were still better for the laparoscopic group [35,36].

Another trial, the COLOR trial was a non inferiority trial that compared laparoscopic colectomy *vs.* open colectomy. Disease-free survival at 3 years after surgery was the primary outcome, with a prespecified non-inferiority boundary at 7% difference between groups. This was a larger trial with 1248 patients. Positive resection margins, number of lymph nodes removed, and morbidity and mortality were similar in both groups. The combined 3-year disease-free survival for all stages was 74.2% (95% CI 70.4-78.0) in the laparoscopic group and 76.2% (72.6-79.8) in the open-surgery group (p=0.70 by log-rank test); the difference in disease-free survival after 3 years was 2.0% (95% CI -3.2 to 7.2), which was well below the pre determined non inferiority boundary of 7%. The difference in overall survival after 3 years was 2.4%, with open colectomy faring better [37,38]. The COST trial also showed similar local recurrence rates and

DFS for both laparoscopic and open surgeries [39]. Similar outcomes were reported in an RCT taken up in Australia and NZ.

The UK MRC CLASICC trial recruited 794 patients of colon and rectal cancer combined (526 laparoscopic assisted and 268 open). Overall, there were no differences in the long-term outcomes. The differences in survival rates were OS of 1.8% (95% CI, -5.2% to 8.8%; P=.55), DFS of -1.4% (95% CI, -9.5% to 6.7%; P=.70), local recurrence of -0.8% (95% CI, -5.7% to 4.2%; P=.76), and QoL (P>.01 for all scales). Higher positivity of the circumferential resection margin was reported after laparoscopic Anterior Resection (AR), but it did not translate into an increased incidence of local recurrence. The trial concluded that successful laparoscopic-assisted surgery for colon cancer is as effective as open surgery in terms of oncological outcomes and preservation of QoL. Long-term outcomes for patients with rectal cancer were similar in those undergoing abdominoperineal resection and AR, and support the continued use of laparoscopic surgery in these patients [40-42].

The COREAN trial from South Korea compared open surgery with laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy. Patients with cT3N0-2 mid or low rectal cancer without distant metastasis after preoperative chemoradiotherapy were enrolled at three tertiary-referral hospitals. Patients were randomised 1:1 to receive either open surgery (n=170) or laparoscopic surgery (n=170). Involvement of the circumferential resection margin, macroscopic quality of the total mesorectal excision specimen, number of harvested lymph nodes, and perioperative morbidity did not differ between the two groups. The laparoscopic surgery group showed earlier recovery of bowel function than the open surgery group. They concluded that Laparoscopic surgery after preoperative chemoradiotherapy for mid or low rectal cancer is safe and has short-term benefits compared with open surgery; the quality of oncological resection was equivalent [43].

The COLOR II trial, published in 2013, was a non-inferiority phase 3 trial that compared laparoscopic and open surgery in patients with rectal cancer. They concluded that in selected patients with rectal cancer treated by skilled surgeons, laparoscopic surgery resulted in similar safety, resection margins, and completeness of resection to that of open surgery, and recovery was improved after laparoscopic surgery [44].

The ACOSOG Z6051 Randomized Clinical Trial was undertaken to determine whether laparoscopic resection is noninferior to open resection, as determined by gross pathologic and histologic evaluation of the resected proctectomy specimen. In contrast to the equivalent clinical outcome that was shown by the above mentioned trials in ca rectum, pathologic evaluation did not show non inferiority. Successful resection occurred in 81.7% of laparoscopic resection cases (95% CI, 76.8% to 86.6%) and 86.9% of open resection cases (95% CI, 82.5% to 91.4%) and did not support noninferiority (difference, -5.3%; 1-sided 95% CI, -10.8% to ∞; P for noninferiority=.41). Negative circumferential radial margin was observed in 87.9% laparoscopic resection and 92.3% in open resection group. The use of laparoscopic resection compared with open resection failed to meet the criterion for noninferiority for pathologic outcomes [45].

Also in ALaCaRT RCT, the equivalence of pathologic outcomes was not shown. The primary end point was a composite of oncological factors indicating an adequate surgical resection, with a noninferiority boundary of Δ = -8%. Successful resection was defined as meeting all the following criteria: (1) complete total mesorectal excision, (2) a clear circumferential margin (≥ 1 mm), and (3) a clear distal resection margin (≥ 1 mm). Pathologists used standardized reporting and were blinded to the method of surgery. Among patients with T1-T3 rectal tumors, noninferiority of laparoscopic surgery compared with open surgery for successful resection was not established. Although the overall quality of surgery was high, the findings did not provide sufficient evidence for the routine use of laparoscopic surgery [46].

Although there was no doubt that laparoscopic surgery did improve the short term outcomes, it was doubtful whether the benefits of laparoscopy still exist when open surgery is optimized within an enhanced recovery protocol. To answer this question, The EnROL (Enhanced Recovery Open Versus Laparoscopic) trial with 208 patients was undertaken. They concluded that in patients treated by experienced surgeons within an enhanced recovery protocol, physical fatigue and other perioperative outcomes were similar in both groups, but laparoscopic surgery significantly reduced length of hospital stay [47].

From the above trials, it is now clear to us that even though short term clinical outcomes with laparoscopic surgery are excellent, there is still doubts on the long term oncological outcomes given that both the trials that compared the pathological specimens of open *vs.* laparoscopic rectal surgery has termed laparoscopic specimens "inferior" to open resected specimens. Given the confines of the pelvis and limited maneuvreability of laparoscopic instruments, it is quite understandable. So, robotic surgery, with 540 degrees rotation, 180 degrees of articulation and 7 degrees of freedom seemed enticing.

Robotic surgery

Given that surgeons experienced in laparoscopic surgery have a short learning curve and that robotic TME may attenuate the long and steep learning curve of laparoscopic TME [48,49], there has been a keen interest in robotic rectal surgery. Some studies state equivalence of robotic to laparoscopic surgery whereas it is seen in various meta analyses that robotic surgery has less conversions to open than the laparoscopic surgery while cost and longer operative times have been a concern [50-53]. ROLARR trial was a multicentric RCT which sought to find out if the conversion rate in robotic surgery for rectal cancer is better than laparoscopy as the primary outcome and various pathologic and short term surgical outcomes as the secondary outcome. Contrary to the expected outcome, it concluded that robotic-assisted laparoscopic surgery, as compared with conventional laparoscopic surgery, did not significantly reduce the risk of conversion to open laparotomy and there was no statistically significant differences in secondary clinical outcomes [54]. Although robotics find a special place in rectal cancer and lot of research is there related to it, its role in colon cancer is still not established. Although robotic surgery can be done, it confers no special advantage to the surgeon, except in some cases where greater maneuverability is required due to anatomical constraints.

SILS (Single Incision Laparoscopic Surgery): SILS have been described for colon carcinoma. Although right hemicolectomy is technically less challenging, left colon and transverse colon cancer resection has been problematic. It is technically feasible in small tumours, lean patients and more useful for segmental resection and right hemicolectomy [55-58]. The oncological safety of SILS has not yet been proven although a few studies do show equivalence of SILS to conventional laparoscopic techniques. SILS have not gained ground

in the management of ca rectum due to difficulties with instrument movement, rectal transection and challenge of double stapling of anastomoses intracorporeally.

Endoscopic techniques

These include TEM (Transanal Endoscopic Microsurgery), TAMIS (TransAnal Minimally Invasive Surgery) and TaTME techniques. They can be clubbed under NOTES for colorectal surgery. The first endoscopic transanal surgery was done by Buess in 1983. Clancey et al. [59] in a meta analysis, showed better oncological outcomes with endoscopic transanal surgery rather than with traditional transanal excision methods.

TEM/TAMIS - The principles of both these techniques are essentially same. They only differ on the type of ports and equipments used. TEM uses a highly sophisticated unit with specialized instruments whereas TEMIS uses existing conventional laparoscopic ports and instruments. Both of these techniques have several advantages over conventional transanal excision. Conventional transanal surgery uses rigid instruments and specialized retractors whereas TEM/TAMIS uses camera and endoscopic/laparoscopic instruments which gives superior maneuverability for making full thickness rectal wall resections. Again, rigid instruments can give a good vision with good instrument maneuverability only upto 10 cm whereas surgery is possible on TEM/TAMIS platform till 15 cm to 20 cm. Since it has the drawback of excising only the primary tumour without addressing the lymph nodes, it is suitable for only those patients whose nodes are clinically free or whose nodes need not be addressed.

The following indications have been recommended by various surgical societies, including the American Society of Colon and Rectal Surgeons (ASCRS):

• Lesions smaller than 3 cm; however, a study by Khoury reported the use of TEM to treat benign rectal lesions in the range of 5 cm to 8 cm.

• Mobile lesions.

• Polypoid lesions.

• Anatomically accessible lesions localized to the bowel wall (T1N0).

• Lesions confined to the extraperitoneal region of the rectum.

• Lesions occupying less than 40% of the circumference of the bowel lumen; however, the use of TEM for giant circumferential rectal adenomas has been reported.

• Well-differentiated or moderately differentiated lesions.

• Lesions not associated with lymphovascular invasion.

• Transanal TME (TaTME): It combines the principles of TEM, TME and sphincter salvage surgery. It basically addresses the problems.

• Inability of TEM/TAMIS to address lymph nodes - mesorectal fascia.

• Hard-to-access anatomical areas which would be impossible to reach by means of standard laparoscopic approaches, especially in male patients with a high BMI and low rectal cancer, thus resulting in open surgery.

It has most commonly 2 teams operating simultaneously-One through the transanal route for full thickness resection of the rectal wall. Another team mobilises the rectum laparoscopically and ligates the inferior mesenteric vessels and addresses the corresponding lymph nodes. Also, pelvic node dissection is possible in case the surgeon decides to do so with this approach. Here sphincter salvage surgery is better performed due a magnified field and subsequent better delineation of the surgical planes. It also gives better visualization of the pelvic nerve fibres, which gives the theoretical advantage of better bowel and bladder functions [60].

Although the guidelines are believed to represent the optimal treatment strategy, when appropriate the patients should preferably be included in a clinical trial over accepted or standard therapy.

NCCN guidelines on minimal access surgery on carcinoma of the colon and rectum

Colon - Laparoscopic surgery is an option in cases where the polyp specimen is fragmented, the margins cannot be assessed or the specimen shows unfavourable histology. Here, colectomy with en bloc removal of LN is recommended. Laparoscopic surgery is also an option for curative and palliative surgeries of the colon. In fact, laparoscopic surgery is preferable given better short term outcomes in palliative settings.

Rectum - Some studies have shown that laparoscopy is associated with similar short and long term outcomes when compared to open surgery, where as other studies have shown that laparoscopy is associated with higher rates of circumferential margin positivity and incomplete TME. So MIS is considered based on the following principles.

• The surgeon should have experience in performing MIS with TME.

• Not indicated in threatened or high risk circumferential margin based on imaging. For these high risk tumours, open surgery is preferred.

• Not generally indicated for acute bowel obstruction or perforation from cancer.

• Thorough abdominal exploration is required.

Robotic surgery for colorectal cancer: The laparoscopic *vs.* robotic surgery studies have mostly been observational cohort studies. Robotic approach appears to result in longer operating times and is more expensive but may be associated with less blood loss, shorter time to recovery of bowel function, shorter hospital stays and lower rates of complications and infections.

NCCN criteria on transanal excision

• <30% of the circumference of the bowel.

• <3 cm size.

• Margin clear >3 mm.

• Mobile no fixed.

• Within 8 cm from the anal verge.

• T1 only.

• Endoscopically removed polyp with cancer or indeterminate pathology.

- No LVI or PNI.

- Well to moderately differentiated.

- No evidence of lymphadenopathy on pretreatment imaging.

- Full thickness excision must be feasible.

TEM/TAMIS - When lesion can be adequately localized to the rectum, local excision of more proximal lesions can be technically feasible using advanced techniques such as transanal microscopic surgery or transanal minimally invasive surgery (TAMIS).

ESMO Guidelines

Colon: Laparoscopic colectomy can be safely carried out for colon cancer, particularly for left sided colon cancer. For right sided colonic cancers, the benefit is less obvious since anastomosis must be hand sewn, which requires laparotomy. Laparoscopic approach should be carried out only if the following criteria are met.

- Technically experienced surgeons.

- Lack of serious abdominal adhesion due to prior major abdominal surgery.

- No locally advanced disease and/or acute bowel obstruction or perforation.

Rectum - In selecting laparscopic or open surgery, the surgeon should take into account his/her experience in the technique. TaTME may facilitate pelvic and distal mesorectal dissection but standardization and assessment of the technique is necessary. Robot assisted rectal surgery provides some advantages for the surgeons compared to conventional laparoscopy but is still under evaluation.

ESMO take on TEM - Appropiate as a single modality for early cancers (cT1N0 without adverse features like G3, V1, L1). Only patients with cT1N0 should be considered for such treatment, although TEM for advanced T stage may be appropriate for patients at high surgical risk after discussion with the patient.

TEM permits more accurate en bloc, full thickness local excision of rectal tumours than local excision, and can provide similar oncological results in pT1sm1 (clinical cN0) rectal cancers compared with results achieved by TME, without compromising anorectal function. Local recurrence often occurs in the tumour bed. If there is unfavourable pTNM assessment following local excision, the value of adjuvant CRT in preventing local recurrence is unproven and TME should remain the standard salvage option.

Japanese guidelines - JSCCR 2016

The Japanese guidelines differ from the Western guidelines significantly.

Endoscopic treatment: General principles underlying the indications for endoscopic resection - Only when there is little possibility of lymph node metastasis, and the size and location of the tumor make en bloc resection possible.

Indication criteria for endoscopic resection:

1. Intramucosal carcinoma or carcinoma with slight submucosal invasion.

2. Size does not matter.

3. Any macroscopic type.

Endoscopic treatment methods consist of polypectomy, Endoscopic Mucosal Resection (EMR), and Endoscopic Sub mucosal Dissection (ESD).

Local excision is indicated for cTis (M) cancer and cT1 (SM) cancer (slight invasion) located distal to the second Houston valve (peritoneal reflection).

Lateral lymph node dissection is indicated when the lower border of the tumor is located distal to the peritoneal reflection and the tumor has invaded beyond the muscularis propria.

The indications for laparoscopic surgery are determined by considering the surgeon's experience and skills, as well as tumor factors, such as the location and degree of progression of the cancer, and patient factors, such as obesity and history of open abdominal surgery.

There is no mention regarding robotic surgery.

ICMR consensus document: Mentions endoscopic treatment for pT1 - for T1, grade 1/2 and for those for whom negative margins can be achieved. There is no mention of MIS procedures.

MIS in gynaecologic oncology

MIS has become the standard for the management of uterus confined ca endometrium. Although there had been great enthusiasm regarding use of MIS in ca cervix, the recent LACC trial has however, dampened the enthusiasm and brought an abrupt end to the journey of MIS in ca cervix. Although there has been quite a few speculations regarding the failure of this trial, the progress of MIS will be tardy in this field nonetheless.

Ca endometrium

MIS is the standard for Ca endometrium. Many patients with endometrial cancer are obese and Minimally Invasive Surgery (MIS) is especially advantageous in these patients in reducing postoperative wound complications. Robotic surgery with 3D vision and better maneuverability, especially in limited space such as the pelvis can lead to better dissection.

Since the 1990s, a lot of studies were undertaken - some retrospective analyses, some prospective observational and some RCTs, which showed short term advantages for minimally invasive techniques, along with oncologic equivalence for both the approaches. High quality evidence began to emerge post 2008, with the publication of the short term outcomes for the largest RCT - the LAP2 trial.

LAP2 trial: Patients with clinical stages I to IIA uterine carcinoma/sarcoma were randomly allocated (2:1) to laparoscopy versus laparotomy for hysterectomy, salpingo-oophorectomy, pelvic cytology, and pelvic and para-aortic lymphadenectomy. The study was originally designed to compare perioperative adverse events and Quality of Life (QOL) between laparoscopy and laparotomy over an 8-week postsurgical follow-up period. In 2001, the protocol was amended to extend follow-up to 5 years and add the primary study endpoint of non inferiority of recurrence-free interval, defined as a hazard ratio of 1.4 for laparoscopy relative to laparotomy. The patients were randomly allocated to laparoscopy (n=1,696) versus laparotomy (n=920). There were 309 recurrences (210 laparoscopy; 99 laparotomy) and 350 deaths (229 laparoscopy; 121 laparotomy). The estimated hazard ratio for laparoscopy relative to laparotomy was 1.14 (90% lower bound, 0.92%; 95% upper bound, 1.46), falling short of the protocol-specified definition of noninferiority. However,

the actual recurrence rates were substantially lower than anticipated, resulting in an estimated 3-year recurrence rate of 11.4% with laparoscopy and 10.2% with laparotomy, or a difference of 1.14% (90% lower bound, 1.28%; 95% upper bound, 4.0%). The estimated 5-year overall survival was almost identical in both arms at 89.8%. The trial concluded that the potential for increased risk of cancer recurrence with laparoscopy versus laparotomy was quantified and found to be small and additionally, laparoscopy group had significantly better short term outcomes [61,62].

The Laparoscopic Approach to Cancer of the Endometrium (LACE) trial was a large, multinational randomized trial (n=760) of women with stage I endometrioid EC who underwent staging with TLH or total abdominal hysterectomy (TAH) and found no difference in disease-free survival at 4.5 years (81.6 versus 81.3 percent) or overall survival (mortality: 7.4 versus 6.8 percent). This was the second largest trial to evaluate this question [63].

A subset of 361 participants were enrolled in a QOL study [64]. Patients in the TLH group reported significantly greater QOL compared with those who had TAH in the initial postoperative period. For some patients, the improved QOL persisted up to six months after surgery and continued to favor TLH.

In 2012, a meticulous meta analysis of laparoscopic procedures for early stage ca endometrium was done by Galaal et al. [65]. This review found evidence to support the role of laparoscopy for the management of early endometrial cancer. They concluded that for presumed early stage primary endometrioid adenocarcinoma of the endometrium, laparoscopy is associated with similar overall and disease-free survival. Laparoscopy is associated with reduced operative morbidity and hospital stay. However, there was no significant difference in severe post-operative morbidity between the two modalities.

Robotic surgery, with its advantages is expected to overcome the constraints of working in closed spaces in laparoscopy. Robotic is better for obese and morbidly obese patients. For both the obese and morbidly obese patient, robotic surgery was associated with shorter operative time, less blood loss, increased lymph node retrieval and shorter hospital stay [66]. However, despite claims of decreased complications with robotic hysterectomy, other studies found similar morbidity but increased cost compared with laparoscopic hysterectomy [67,68]. A randomized trial (n=99) of robotic versus laparoscopic staging for EC found shorter operative duration for robotic group (139 minutes *vs.* 170 minutes). There were no conversions to laparotomy in the robotic group compared with 5 of 49 cases in the laparoscopy group. There were no differences in the number of lymph nodes removed, bleeding, or the length of postoperative hospital stay. The rate of major postoperative complications showed no statistically significant difference in robotic surgery versus laparoscopy (10 versus 22 percent) [69].

The outcomes do lead us to a conclusion that robotic surgery does increase the surgeon comfort as evident from the fact that it is better suited for obese patients and lesser open conversions. Although the short term outcomes might be better, the costs associated with robotics might make acceptance for robotic surgery as a routine quite tardy. There is no high level evidence for long term outcomes and surgical superiority for robotic surgery.

NCCN guidelines state that TAH + BSO and lymph node assessment may be performed by any surgical route (e.g. Laparoscopic, robotic, vaginal, abdominal) although the standard in those with uterine confined disease is to perform the procedure with minimally invasive techniques. Regarding lymph node dissection, NCCN says that when indicated, surgical staging is recommended to gather full pathologic and prognostic data on which to base decisions regarding adjuvant treatment for select patients who don't have medical or technical contraindications to lymph node dissection. NCCN also supports the use of sentinel lymph node staging and has laid down the principles for conducting the SLNB.

The SGO (Society of Gynaecologic Oncology) and ICMR has also issued guidelines on the lines of NCCN guidelines in support of use of minimally invasive techniques for ca endometrium and SLNB.

Ca cervix

The road to use of MIS techniques for management of early stage ca cervix has been interesting. Prior to the LACC trial, all previously conducted retrospective studies uniformly concluded that MIS led to better short term outcomes and equivalent oncological outcomes [70,71]. MIS techniques, especially laparoscopy was very much in vogue since 2000 and an MIS was a standard practice in an in increasing number of institutions for early stage ca cervix. Some studies found robotic surgery to be better than laparoscopy [72-74].

The LACC (Laparoscopic Approach to Cervical Cancer) trial was undertaken since there are limited data from retrospective studies regarding whether survival outcomes after laparoscopic or robot-assisted radical hysterectomy (minimally invasive surgery) are equivalent to those after open abdominal radical hysterectomy (open surgery) among women with early-stage cervical cancer. The primary outcome was the rate of disease-free survival at 4.5 years, with non inferiority claimed if the lower boundary of the two-sided 95% confidence interval of the between-group difference (minimally invasive surgery minus open surgery) was greater than -7.2 percentage points. The rate of disease-free survival at 4.5 years was 86.0% with minimally invasive surgery and 96.5% with open surgery, a difference of -10.6 percentage points (95% confidence interval [CI], -16.4 to -4.7). Minimally invasive surgery was associated with a lower rate of disease-free survival than open surgery (3-year rate, 91.2% *vs.* 97.1%; hazard ratio for disease recurrence or death from cervical cancer, 3.74 [75].

This trial failed to show non inferiority for MIS procedures. Approximately 42 percent of trial participants had tumors ≥ 2 cm; however, the authors noted that the trial was underpowered to evaluate outcomes for tumor size <2 cm or other low-risk features (no LVSI, <10 mm depth, no lymph node involvement).

In a cohort study of women with stage IA2 or IB1 cervical cancer who underwent radical hysterectomy, 1225 patients underwent MIS compared with 1236 who underwent open surgery; to achieve two groups with similar characteristics, the groups were weighted based on a propensity score (the probability of MIS). With a median follow-up of 45 months, MIS was associated with a higher four-year mortality rate (9.1 versus 5.3 percent). Subgroup analysis found an increased HR for mortality with MIS for robotic procedures, squamous cell and adenocarcinoma, and tumor size ≥ 2 cm; there was a trend toward higher mortality in traditional laparoscopic procedures (this was nearly statistically significant). The study was underpowered to detect a difference in mortality risk in tumor size <2 cm (HR 1.46, 95% CI 0.70-3.02) [76].

Based on the above recent data, MIS procedures for tumour >2 cm is not recommended by most authorities, although it might have

some role in management of smaller tumours (<2 cm) and those without high risk features. This recommendation is also based on the fact that tumour size divided in 2 cm intervals is the most important predictor for recurrence [77].

NCCN guidelines state that given recently presented findings of significantly poorly survival outcomes with the MIS approaches compared to the open approach in an RCT of women of early stage cervical cancer, women should be carefully counselled about the short term *vs.* long term outcomes and the oncologic risks of different surgical procedures. They also state that radical vaginal trachelectomy with laparoscopic lymphadenectomy procedure (with or without SLN mapping) offers a fertility sparing option for carefully selected individuals with stage IA2 or stage IB1 lesions. The cervix, upper vagina and supporting ligaments are also removed as with a type B radical hysterectomy, but the uterine corpus is preserved.

Ca ovary

Minimally invasive surgery - laparoscopy and robotic surgery has not attained widespread acceptance in surgical management of ca ovary due to the fact that >80% of the patients present at an advanced stage and owing to certain controversial issues like.

1.   The cystic nature of the neoplasms arising from the ovary and the concomitant danger of rupture during extraction via the laparoscopic ports or smaller extraction incisions.

2.   Accuracy of laparoscopic surgical staging - concern regarding adequacy of lymph node harvest laparoscopically.

3.   Possibility of port-site metastasis.

Rather, it is now increasingly used to stage and determine the extensiveness of deposits/disease burden in ca ovary and determine if optimal cytoreduction can be achieved.

1990 Reich et al. [78] became the first to report a case of laparoscopic surgery for stage I ovarian cancer, and in 1994 Querleu and LeBlanc et al. [79] performed laparoscopic surgery in a series of 9 cases of ovarian cancer and fallopian tube cancer and assessed the feasibility of laparoscopic paraaortic lymphadenectomy. These have been followed by many reports on the feasibility of laparoscopic surgery in the treatment of early ovarian cancers. A few studies and meta analyses have found oncologic equivalence in early ovarian cancer (Stage I) [80-83] whereas some authorities found no good-quality evidence to help quantify the risks and benefits of laparoscopy for the management of early-stage ovarian cancer as routine clinical practice [84]. Again one meta analyses failed to show oncological safety and recurrence *via* MIS procedures [85].

The use of laparoscopy for determination if optimal cytoreduction can be achieved is the most established, given the limitation of imaging to correctly determine the peritoneal disease load. Determination of the disease load becomes important in taking decisions regarding neoadjuvant chemotherapy. Fagotti laparoscopy-based score (PIV - Predictive Index Value) is a useful predictor of optimal cytoreduction [86-88]. The PIV is based on the extent of peritoneal carcinomatosis, diaphragmatic disease, mesenteric disease, omental disease, bowel infiltration, stomach infiltration and liver metastasis. A PIV score of ≥ 8 was 100% predictive of suboptimal cytoreduction. A multicenter RCT (LapOvCa-trial) has demonstrated the efficacy of laparoscopy in prediction of optimal cytoreduction, but the criteria used was different from what was used by Fagotti [89].

Although there is no high quality evidence to support the use of laparoscopy in early stage ovarian cancer, in view of plenty of studies of lower level of evidence supporting its use, the NCCN has endorsed its use in the management of early staged ovarian cancer in the hands of an experienced surgeon and in cases of limited disease post neoadjuvant chemotherapy. NCCN also states that laparoscopy can be used in select patients to evaluate whether optimal cytoreduction can be achieved.

TORS (Transoral Robotic Surgery) and TLM (Transoral Laser Microsurgery)

With the rapid in roads that was made into surgical branches by the robot, it was made clear that head and neck surgery would not be left far behind. Robotic surgery was first used in 2005 for benign pharyngeal cyst, it has now found its utility in the field of oncology where it is not possible to reach the tumour with conventional surgery. Transoral Robotic Surgery is basically used in tumours of the hypopharynx and the larynx. With the increase in HPV related hypopharyngeal cancers and development of new techniques of node dissection, this field has turned exciting. TLM - Transoral Laser Microsurgery is the use of LASER for resection of mainly laryngeal tumours but it can also be used for other head and neck tumours.

Hypopharyngeal cancers which are HPV related has a special place for TORS/TLM for the following reasons.

•   Surgery alone is curative in this subgroup. A margin of 1.5 mm to 2 mm is deemed adequate (NCCN guidelines).

•   Mostly in young patients and have better prognosis. They live long enough for the long term effects of RT to set in. TORS/TLM can avoid these sequelae by avoiding RT altogether or by management with lower doses of radiation.

•   If surgery is planned for patients of oropharyngeal cancer, TORS/TLM has the following advantages irrespective of the HPV status.

•   No mandibulotomy or lip splitting incision used - lesser swallowing or speech derangement [90], and better cosmesis.

•   Ability to preserve voice.

•   More patient satisfaction and lesser pain scores.

•   Ability to visualize the whole tumour due to visual aids and magnification, which also leads to better visualization of the margins and consequent less margin positivity rates.

•   No need of long term feeding tubes - feeds can be commenced by the second week.

•   Most of the patients can be spared tracheostomy.

TLM

In 1972, Strong and Jako coupled a CO_2 laser to a surgical microscope for use through a laryngoscope [91]. They first used it for benign procedures. Three years later, in 1975, Strong used the CO_2 laser to successfully treat 11 patients with early T1 laryngeal cancer [92]. Subsequently, researchers developed sturdy instruments to better visualize and manipulate the larynx for resection. The recent introduction of flexible hollow tubes to deliver laser beam has added to the maneuverability and ease of tumour resection. A recent meta-analysis of 16 studies, none randomized has found that for T1 glottic carcinoma, TLM is the superior modality in terms of overall survival,

disease specific survival and laryngeal preservation [93]. NCCN has mentioned TLM is a method for endoscopic removal of glottis and supraglottis cancer in Tis, T1 - T2 and select cases of T3.

TORS

First approved by US FDA for the use in oropharyngeal tumours and obstructive sleep apnoea, its use has rapidly increased, particularly in the United States of America. The NCCN has endorsed its use in cancers of the oral cavity, pharynx and the larynx. A number of meta analyses have reported TORS to be less time-consuming, more acceptable to the patients, and having less complications as compared to the more invasive techniques while being oncologically safe involving conventional surgery although the quality of this evidence is limited [94-96].

'Early-stage squamous cell carcinoma of the oropharynx : radiotherapy versus trans-oral robotic surgery (ORATOR)' is a phase II randomised controlled trial comparing primary radiation therapy with primary transoral robotic surgery for small-volume primary (T1-2, N0-2) OPSCC. It is currently in progress with an estimated completion date of June 2021. The result of QOL (Quality of life) post 1 year after therapy is out and it showed better QOL scores for the RT arm although not statistically significant [97]. Another trial 'European Organisation for Research and Treatment of Cancer 1420 (EORTC 1420-HNCG-ROG)' is a phase III, randomised study assessing the "best of" radiotherapy compared to transoral robotic surgery/ transoral laser microsurgery in patients with T1-T2, N0 squamous cell carcinoma of the oropharynx and base of tongue is ongoing.

Ca thyroid

Minimally Invasive Video Assisted Thyroidectomy (MIVAT)/ Minimally Invasive Thyroid Surgery (MATS) although the terminology suggests 'minimally invasive', it is far from true, which is in fact a remote access procedure, except the trans-cervical approach. It was originally conceived to rid the neck of a scar and instead approach the thyroid *via* alternate incisions which can be concealed. In the quest to superior cosmetic outcomes, laparoscopy has ended up with remote incisions but at the cost of more tissue dissection than an open thyroidectomy would warrant. So, it is also called endoscopic thyroidectomy or remote access thyroidectomy. It has to be differentiated from MIT (Minimally Invasive open Thyroidectomy) in that in MIT, the whole procedure is done as in conventional open method but with a smaller incision (<6 cm).

The first endoscopic thyroidectomy was reported in 1997, by Huscher [98]. He used 3 ports at suprasternal notch, at the angle of the mandible and midway between the other two, around 4 cm above the clavicle. All the laparoscopic ports were placed along the anterior border of the sternocleidomastoid and a 30° scope was used. It was done for a FNAC proven benign nodule. Since then, there have been various other techniques that have been described - neck, axilla, transoral (transvestibular and trans - floor of mouth approaches), posterior auricular, breast and chest approaches for both benign and malignant tumours, although trans-axillary and anterior chest wall routes remain favourite extra cervical routes [99-104]. Although the routes of access may vary, the access is invariably done in subcutaneous or subpectoral fascial plane away from the clavicles and in a subplatysmal plane above the clavicles.

The endoscopic thyroidectomy techniques can be broadly divided into 2 categories - video-assisted gasless and purely endoscopic with gas-insufflation methods. Each of the methods has its own advantages and disadvantages. The video assisted gasless technique has the advantage of lesser dissection, prevention of complication associated with gas insufflation and faster learning curve but has the disadvantage of having a small scar in the neck. Again, the totally endoscopic approach has the advantage of avoiding a scar in the neck but at the cost of more dissection and risk of complications associated with gas insufflation.

Robotic thyroidectomy: It was first utilized for transaxillary thyroidectomy by Chung in 2007. Since then a lot of investigators have appreciated the safety and efficacy of robots for thyroidectomy. The utilization of robot is far greater in South Korea, compared to slower acceptance in the West. The Bilateral Axillo Breast Approach (BABA)**,** Transaxillary, retroauricular (facelift) and transoral approaches are most commonly used. Both the transaxillary and retroauricular approaches are performed in a gasless fashion, while the transoral technique requires CO_2 gas insufflation for the procedure. It has the added advantage of being able to carry out neck dissection at the same setting.

American Thyroid Association Statement on Remote-Access Thyroid Surgery was published on 2016. They have laid out the following selection criteria [105].

Factors relating to the patient include: (i) thin body habitus (except for the facelift approach), and (ii) the absence of excessive body fat along the flap trajectory (except for the facelift approach). Factors relating to the thyroid pathology include: (i) well-circumscribed nodule ≤ 3 cm, and thyroid lobe <5 cm to 6 cm in the largest dimension; and (ii) underlying thyroid pathology with no evidence of thyroiditis on ultrasound. Factors relating to specific approaches include the fact that the distance between the axilla and the sternal notch should ideally be <15 cm to 17 cm for an axillary approach. Absolute contraindications include: (i) evidence of thyroid cancer with extrathyroidal extension or lymph node involvement; (ii) Graves' disease; (iii) substernal extension; and (iv) Previous neck surgery. Overall, the ideal patient is a patient with <3 cm unilateral nodule who wishes to avoid a neck scar.

The NCCN and ESMO have not commented on minimal access surgery in thyroid cancers.

Prostate cancer

Minimally invasive surgical procedures for treatment of prostate cancer includes laparoscopic prostatectomy, robotic radical prostatectomy, cryosurgical ablation of the prostate, laser prostatectomy, Transurethral Needle Ablation (TUNA), Transurethral Microwave Thermotherapy (TUMT), Transurethral Electrovaporization (TUVP), Transurethral Incision (TUIP) etc. Here, we'll concentrate on the surgical techniques that are most widely used to achieve cure - laparoscopic and robotic prostatectomy.

Although options for treatment of ca prostate includes both surgery and radiation therapy, both are associated with certain morbidities, although there has been a dramatic reduction of surgical morbidities like blood loss, postoperative pain, long hospitalization duration erectile dysfunction and incontinence after the introduction of minimal access techniques and better understanding of the nerve anatomy.

Radiation therapy has certain disadvantages like inconvenient 7 weeks therapy, higher doses (>81 Gy) commonly used in the treatment of prostate cancer and associated short term problems, long-term

urinary quality of life is adversely affected by irritative symptoms, erectile dysfunction and radiation cystitis.

Laparoscopic Prostatectomy (LRP) was first reported in 1997 which showed the feasibility of the use of laparoscopy in carcinoma prostate [106]. Again, the use of robot was first reported in 2001 [107].This shift was natural considering the steep learning curve for laparoscopic prostatectomy and anatomical constraints of the bony pelvis, where manipulation with laparoscopic instruments was a problem. A recent meta analysis have concluded that the minimal access techniques - Robotic (RARP)/Laparoscopic (LRP) is associated with lower blood loss, transfusion rate and less hospitalization duration. The available data were insufficient to prove the superiority of any surgical approach in terms of postoperative complications, functional and oncologic outcomes [108]. Again, if laparoscopy is compared with robotic, robotic prostatectomy comes out to be better or at least non inferior to laparoscopic and open techniques in terms of oncological outcomes, functional outcomes and surgical margin positivity rates [109-113].

NCCN states that the outcomes of laparoscopic and robotic radical prostatectomy are comparable to open techniques in experienced hands.

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