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Review Articles

The past, the present, and the future of minimally invasive therapy in laparoscopic surgery: A review and speculative outlook

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Abstract
It took nearly a hundred years until laparoscopy overlooked the realm of general surgery, but rarely in the history of surgery did we observe a similar revolution. Few surgical procedures have changed so rapidly and so profoundly the daily activities of each surgeon. As with any innovation, laparoscopy represented a robust incitement to test its application to almost all the abdominal districts and soon demonstrated clear advantages in surgery of the spleen, adrenal gland and the urinary tract. Today laparoscopy has proven to actually be the most important advancement also in colorectal surgery since the introduction of surgical stapling, with large meta-analyses demonstrating undeniable advantages also in rectal cancer treatment. To be true, the concept of minimal invasiveness was first applied to the rectum even earlier than laparoscopy when transanal endoscopic microsurgery (TEM) was introduced into clinical practice, and today represents a modern platform with extending indications. Looking at the future, economy is going to influence strategic social decisions of governments, which will condition the development of new technologies. The significant increase in prevention through screening programs will lead to the diagnosis of a vast majority of early lesions, which will favour a further decrease of invasiveness.

Keywords: Abdominal surgery, minimally invasive surgery, laparoscopic colorectal surgery, NOTES, robotic surgery, TEM

History

It took nearly a hundred years until laparoscopy overlooked the realm of general surgery, but rarely in the history of surgery did we observe a similar revolution. Laparoscopic cholecystectomy has caught on very quickly at the turn of the 1980s and 1990s, quickly becoming the gold standard in the treatment of gallbladder stones. Few surgical procedures have changed so rapidly and so profoundly the daily activities of each surgeon.

The first “open” cholecystectomy of which we have news was executed on July 15, 1882, by the German surgeon Carl Johann August Langenbuch (1846-1901) at the Lazarus Krankenhaus, Berlin, on a 43-year-old man. The history of laparoscopy is not that more recent. First report is dated 1901, when the Russian gynecologist Dimitri Ott examined the peritoneal cavity of a pregnant woman using a mirror and a speculum introduced through a culdoscopic opening (1,2). In the following years the Swedish surgeon Hans Christian Jacobaeus reported 72 patients undergoing inspection of the abdominal and thoracic cavities over a period of ten years, coining the terms “laparoscopy” and “thoracoscopy”, from the greek “*lapara*”, i.e. *abdomen*, “*thoraco*”, i.e. *chest* and “*skopein*”, i.e. *to see* (3). Finally, it was George Bercy, an American surgeon, who first had the idea to attach a camera to the laparoscope. It was 1962 and the era of video laparoscopy had begun.

This contributed consistently to transform laparoscopy from a mere simple diagnostic tool into a therapeutic technique. These were the years in which laparoscopy seemed always to be characterized more as a branch of gynecology, because this was the field that seemed to offer the greatest advantages of its application. This also explains why the leading experts in endoscopic technique in those years almost all belong to the field of gynecology. One of these, Kurt Semm, was the first, although gynecologist, to propose and execute, on September 12, 1980, a laparoscopic appendectomy (4).

There is uncertainty about the actual authorship of the first laparoscopic cholecystectomy. There are traces of a publication in 1983 by the Russian Lukichev describing the technique, but due to the use of the Russian language, the text remained unknown for years (5). Unaware of this, Erich Muhe claimed the execution of the first laparoscopic cholecystectomy on September 12, 1985 (6–8). However, his description of the technique did not gain the favours of the German scientific society, and it was ignored for months, and subjected to severe criticism. It was March 17, 1987 when Philippe Mouret performed his first laparoscopic cholecystectomy in Lyon, France (9). This is the date to which you can actually trace the beginning of laparoscopy in general surgery. It actually represents a milestone in the history of surgery, although Philippe Mouret reported his experience as quite natural, without premeditation. It was a 50-year-old patient who suffered from pelvic adhesions, who was referred to him for an intervention of laparoscopic adhesiolysis. However, the patient was also suffering from symptomatic gallstones and had asked him if it was not possible to perform both actions simultaneously. So Mouret performed an initial exploration of the liver lodge, which turned out to be easy due to the thinness of the patient. At that time, moreover, he had already racked up over 8000 laparoscopies and over 100 laparoscopic appendectomies. After adhesiolysis he performed the preparation of the pedicle of the gallbladder rather easily, and he felt sure enough that he completed the cholecystectomy under laparoscopic conditions.

Since that date, the cases began to occur with a certain continuity in the following weeks. Nevertheless, it took a few more years before the technique was recognized by the scientific world for its extraordinary importance, so as to be indicated by some as the “Second French Revolution”. It was estimated that the percentage of cholecystectomies done laparoscopically reached 80% in 1992; such a rapid acceptance of a new surgical technique had never been seen before (10). The technique described by the authors was henceforth called the “French” technique, different from that adopted by colleagues from overseas. In fact, the experience of laparoscopic cholecystectomy started a little later in the United States, namely with the work of Barry McKernan and William Saye who performed the first laparoscopic cholecystectomy in the US on June 22, 1988 in Marietta, Georgia (11). They were soon followed by the most well-known Eddie Reddick and Douglas Olsen in Nashville, Tennessee (12), who, in addition to being known for some successful endoscopic instruments conceived by them, are those who developed the technique now known as “American”, characterized by a different positioning of trocars to achieve a different approach to the organs.

This was just the beginning of a dramatic change in almost all the fields of surgery, deeply influencing the way surgeons act and think, and changing the way patients are cured. Several questions were continuously discussed during this quarter of a century, but lack of evidence did not allow coming to clear conclusions. They can be categorized into two major classifications, one regarding the application of the concept of minimal invasiveness to the different abdominal districts, the other regarding the development and fruitful application of innovative technologies which might influence the development of novel techniques. In the following paragraphs we would like to review where we were, where we are and where we will probably be in respect to these two different characterisations.

The evolution of techniques

As for any innovation, laparoscopy represented a robust incitement to test the feasibility of its application to almost all the abdominal districts. Laparoscopy soon demonstrated its clear advantages in surgery of the spleen, adrenal gland and the entire urinary tract, while possible advantages in gastric resection following oncologic criteria, as well as in liver and pancreas resections, if not of limited entity, are still debated and did not meet much favour from the scientific community. Undoubtedly, the abdominal district in which minimal invasiveness has demonstrated the clearest advantages over the years is the large bowel.

For a long time colorectal surgeons seemed immune to the contagious excitement which surrounded the development of laparoscopic surgery across the 1980s and 1990s, ignoring the unique patient

benefits if not refuting them. Colorectal surgery lagged behind, as the challenges of working in multiple quadrants with the need for extensive vascular control within an often thick friable mesentery, the requirement of anastomosis, and the surgical indications such as inflammatory bowel disease and neoplasia dampened enthusiasm (13). Reports of port site metastases further decelerated the adoption of the techniques and the proliferation of the procedures (14). Finally after the clinical outcome of surgical therapy (COST) trial was presented at the May 2004 meeting of the American Society of Colon and Rectal Surgeons (ASCRS) and simultaneously published in the New England Journal of Medicine (15) did acceptance accelerate.

Following the introduction of surgical stapling, laparoscopy has proven to actually be the most important advance also in colorectal surgery today (16). Oncologic safety has now been demonstrated for laparoscopy-assisted surgery for colon adenocarcinoma after three and five years of follow-up. Pooled data from large multicenter and smaller single-center trials demonstrate that the modality conveys significant short-term benefits as compared with open surgery, although its full potential has probably not yet been reached. Currently, the data support improvements in wound morbidity, intraoperative blood loss, narcotic analgesia requirements, time to resumption of bowel movements, and time to discharge from hospital. There is a large potential for improved short-term results when combined with current and developing enhanced-recovery programs.

To be true, the concept of minimal invasiveness was first applied to the rectum even earlier than to the appendix and the gall bladder. It was in 1983 when transanal endoscopic microsurgery (TEM) was introduced into clinical practice by Gerhard Buess in Germany, as a novel surgical approach for the resection of large rectal adenomas (17). This procedure encompassed general anesthesia, while now it is more often performed under spinal anesthesia, and the use of expensive specialized equipment with 3D vision from Richard Wolf (Knittingen, Germany), which is now more often replaced by the cheaper and more user-friendly 2D equipment from Karl Storz (Tuttlingen, Germany). Since its introduction, many surgical practices have adopted TEM as the new standard therapy for large rectal adenomas (18). Transanal endoscopic microsurgery (TEM) was originally conceived for the treatment of large sessile extraperitoneal rectal adenomas, step by step expanding its indications. First it proved curative for “low risk” rectal cancers, as often discovered post-operatively on the resected specimens of preoperatively assessed benign lesions (19,20). Then it earned a role in the palliative treatment of advanced invasive cancers (21,22). In this boundary, today TEM is considered a modern platform for extended indications, such as the resection of intraperitoneal as well as circumferential lesions, and it is combined with sentinel lymph node sampling techniques to determine the indication for a more extensive surgical approach in N+ cancers; recently the transanal approach has been proposed as a complementary technique in combination with the abdominal approach, for the curative sphincter-sparing treatment of invasive bulky and low rectal cancer (23).

While it took 30 years to asses the role of TEM for the resection of benign and selected malignant neoplasms of the rectum, after more than 20 years since the first report of laparoscopic colorectal surgery (24), its employment in the treatment of rectal diseases is still debated. Where TME and a systematic lymphadenectomy are considered the main steps of curative therapy of rectal cancer (23), available data are not sufficient to reach any reliable conclusion to date. We recently performed a meta-analysis on available data regarding short-term morbidity after open and laparoscopic excision, and the most interesting finding was that the incidence of mortality showed a significant reduction in the laparoscopic group compared to open surgery. Furthermore, the overall incidence of post-operative complications was also significantly lower in the laparoscopic group with a RR of 0.81. The analysis of all included studies showed a clear advantage for laparoscopy also in the specific analysis of both surgical and medical complications, which translated, as already shown in the treatment of colon cancer (15,25–27), into a clear advantage in terms of an earlier bowel activity restoration, time to oral intake and duration of postoperative hospital stay, whereas the only clear disadvantage was represented by the relatively longer operative time. A similar analysis was then repeated limiting the object of the study to patients affected by extra-peritoneal

rectal cancer, where we also proved that laparoscopic rectal resection appears to have clinically measurable short-term advantages in patients with primary resectable rectal cancer. Although technically demanding, laparoscopic rectal resection is safe and guarantees a faster recovery. We then focused on the oncologic adequacy of the laparoscopic technique compared to open rectal resection. There is no doubt that cancer patients have as principal aim to be cured from their disease, regardless of the technique, so that they are prone to banish advantages of minimally invasive treatment if they do not correspond to comparable oncologic effectiveness. For this reason, the present analysis is of even greater importance than the previous one, to identify the correct path to move forward in the application of the concept of minimal invasiveness in this field. The main finding of this meta-analysis was that the involvement of the circumferential margin, i.e. <1 mm, was reported in 8.0% of the patients in the laparoscopic group and in 12.7% in the open group, with an overall relative risk (RR) 0.68, although this result was deeply influenced by Lujan 2012 (28), nor was it confirmed both in the sensitivity analysis of randomized controlled trials (RCTs) and in the subgroup analysis of only extraperitoneal series, and should therefore be taken with caution. Moreover, the number of lymph nodes, the average distal margin and its involvement, the average circumferential margin, the rate of R0 resections and the mesorectal fascia integrity as assessed by the pathologist, showed no significant differences between the two groups. Even the local recurrence rate at five years resulted similar in the laparoscopic group and the open group, so that in conclusion, although technically demanding, laparoscopic rectal resection appears to be equally effective in terms of oncologic adequacy, in selected patients with primary resectable rectal cancer.

The evolution of technologies

In general, the introduction of laparoscopy entailed the need of selection of patients, as it represented an increase in technical difficulties, which could result in the impossibility to proceed laparoscopically in particular anatomic conditions. In all cases, in endoscopic surgery, the ability to guide the instrument is significantly decreased compared with open surgery. Rigid laparoscopic instruments offer only four of the six degrees of freedom required for the free handling of objects in space. Laparoscopy represented a worsening of tissue manipulation, which might reflect on suboptimal vision due to insufficient tissue retraction and exposure. For this reason, since the early 1990s the idea to use robotic technology to improve this limit of laparoscopy has been presented. Robotics technology can be used to restore full mobility of the endoscopic instrument. A master-slave manipulator system, named ARTEMIS, for laparoscopic surgery was presented in 1994 by the Research Center Karlsruhe, with the medical advice of Gerhard Buess and Marc Schurr of the University of Tuebingen (29). This prototype consisted of two robotic arms holding two steerable laparoscopic instruments. These two work units were controlled from a console equipped with two master arms operated by the surgeon. The system and its components were evaluated experimentally. Laparoscopic manipulations were feasible with the ARTEMIS system. The placement of ligatures and sutures and the handling of catheters were possible in phantom models. The surgical practicability of the system was demonstrated in animal experiments.

It appeared soon that robotic manipulators were realistic solutions for experimental endoscopic surgery, but their clinical application required further technical development (30). In fact, the project was first moved towards cardiac surgery applications, but even in this district, clinical applications seemed distant. As derivative projects, the group tried to offer solutions for laparoscopic assistance. In fact laparoscopic assistance often demands tiring standing positions and monotonous tasks. The use of mechanical positioning systems derived from open surgery can be unsatisfactory, their movement is often cumbersome and unsafe, since in most cases both hands of the surgeon are required to change position. The use of positioning and holding devices in laparoscopic surgery, in fact, returns direct control of the whole procedure to the operating surgeons, theoretically increasing precision of action.

The Research Center in Karlsruhe led first to the design of the passive system TISKA Endoarm (31) and later to the remote-controlled FIPS Endoarm (32). Although they proved to be advantageous in

ex-vivo studies, compared to human assistance, in terms of safety and cost-effectiveness they remained at the level of prototypes. At the end of the 1990s several other laparoscopic camera-driving systems were devised: The Endoassist (Armstrong Healthcare, High Wycombe, Buck, UK) (33) and the AESOP system (Computer Motion, Goleta, CA, USA) (34) were available on the market. The rapid introduction of several different architecture and interface solutions reflected the growing interest in these developments (35). But all the different systems proposed with helmet controls, infra-red pointers, visual tracking systems and the first voice controlled devices, on the market did not meet the surgeons' interest (36).

At the same time the development of robotic technology had proceeded and a further example was proposed by Intuitive Surgery (Seattle, WA, USA), named Da Vinci. Along the different generations of the device proposed, the system on the one side showed a good appeal, with almost 2000 devices installed world-wide so far, and more than 300.000 procedures performed. On the other side, the system, first proposed for cardiac surgery and general surgery applications, has failed so far to prove any benefit in these restricted areas, being still under evaluation in the pelvic district both for rectal surgery and prostate surgery, with a general feeling that major technology improvement has to be achieved before it can result clinically advantageous.

A further important development which influenced the diffusion of laparoscopy is related to dissection devices. First the introduction of dissectors based on ultrasound technology in the late 1990s, then on radio-frequency technology, revolutionised the application of laparoscopic techniques making them apparently easier and safer. In truth several studies demonstrated the absence of real need of sophisticated dissecting technology in the vast majority of cases, which can be treated instead by simple mono-polar and bi-polar energy dissectors. Nevertheless, the consistent interest of the industry contributed significantly to the diffusion of laparoscopic techniques, in these years, for the evident feedback. This produced a number of events and courses, and delivered a fashion of organising live events with demonstration of products, that although not always scientifically driven, reflected on a consistent spread of knowledge and adoption of novel techniques.

In a similar way, but with less effort, more recently the concept of single port surgery was supported. All the majors previously involved in the challenge on the promotion of the different dissectors, are faced again in promoting these novel devices. Nevertheless, here the leitmotif of promoting technology to make things easier could not be used. Single port surgery evidently represents a worsening of environment conditions, with doubts as to clear benefits for the patients, for which there is still a lack of evidence. For this reason, this, initially addressed like the further step towards less invasiveness, still struggles to emerge and it is not yet clear if it will, in the end (37).

The future

Before disputing about the future of surgery 25 years from now, we have to seriously focus for a while on the possible scenarios that we will face in that time frame. Economy is getting more and more importance in healthcare and is going to influence strategic social decisions of governments even in industrialised and healthy countries. But other factors are going to play major roles such as the diffusion of social media, through which the vast majority of knowledge and awareness will circulate in a sort of self-made healthcare, reducing the role of doctors to that of specialists consulted only on specific questions or for specific manoeuvres, or the continuous research and development of new technologies, which depending on the economic situation might concentrate on high cost or low cost solutions.

In this, gastroenterology in general will see a dramatic change in diagnostic tools (38), with a significant increase in prevention through screening programs, which will lead to a vast majority of early lesions or initial diseases diagnosed. The way of treatment will be influenced as a consequence, with a consistent decrease of invasiveness. In this scenario it is difficult to foresee which will be the role played by surgeons and how their work will appear, whether towards a wider

application of current concepts of minimal invasiveness, i.e. basically laparoscopy, or if towards further reduction of invasiveness, for instance with the adoption of the NOTES® (Natural Orifices Transluminal Endoscopic Surgery) concepts, or maybe a combination of the two. It is likely that a consistent number of cases will be treated with different ablation techniques such as HIFU (High Intensity Focused Ultrasound) or similar techniques, maybe in combination with more specific chemotherapies, such as those derived by molecular genetics.
In truth lay literature and media have focused attention on NOTES since the beginning of 2007 after the first clinical reports, where the concept and feasibility of NOTES have been tested in animal experiments since 2004 (39). The initial experience of transgastric and transvaginal peritoneal access demonstrated both safety and feasibility in the animal model and has been used as the basis to further evaluate and develop the technology of natural orifice surgery (39–47). Later other possible accesses where described as the transrectal, the transvesical and finally the transesophageal.
NOTES is a new type of surgical procedure currently being studied at research hospitals and facilities around the world. The idea of NOTES was developed several years ago in response to the concepts that patients would

- realize the benefits of less invasive surgery by reducing the recovery time,
- experience less physical discomfort associated with traditional procedures and
- have virtually no visible scarring following this type of surgery.

All of these advantages have spurred research and investigation forward, encouraging physicians and researchers to develop new equipment and techniques to use during NOTES procedures. The growing interest and safe introduction of these novel techniques have led to the creation of new scientific societies and committees with the declared aim of regulating research activity through sponsorships and registries (48).
About a decade after its proposal, the general impression is that after an initial explosive enthusiasm for NOTES techniques, the slowed-down development of dedicated platforms and instruments and the ongoing diffusion of single access techniques has mitigated the spread, diffusion and employment of the techniques. Dedicated platforms comprising all surgical instruments needed for visualization, dissection, manipulation and retraction will probably bring the advantage of reproducing a surgical environment through a single translumenal access, thus avoiding the need for transabdominal trocars, i.e. hybrid procedures. It is difficult now to predict what the new barriers will be. But at the same time, once the techniques will be validated, appropriate training and accreditation should be provided by scientific societies through certified experts in the field. Despite this, NOTES implementation into clinical activity is going on, with excellent results although in extremely selected cases (49). Which benefit this would represent for patients is still too early to be assessed, but research on the topic should go on to provide new solutions to technical problems before a real validation is performed.
Some considerations are needed as to what moved the initial enthusiasm. It was not the patients' demand for a further reduction of invasiveness, as it would be reasonable to think. Although the prospective of a no scar surgery would be appealing for any patient, patients are in general already very much satisfied with laparoscopy results, as they are more concerned about wound pain and complications than cosmetics, so that most of the studies fail to demonstrate any advantage in patients' satisfaction comparing laparoscopy, single-port laparoscopy and NOTES. The real driving force behind the development of this new frontier was the industry that imagined the opening of new businesses related to this research activity. When it was soon understood that the research and development to be done to achieve a stable clinical employment of new techniques was much more than initially thought, the interest began to fade. The need generated by the expectation of a further reduction of invasiveness related to the concept of NOTES was soon satisfied with the implementation of single port techniques with the promotion of new tools.

It has been calculated that in the last decade United States research investments in health coming from industry doubled constantly what was sponsored by the government. In a company-driven development it is difficult to believe that any advancement in health care will not be sustained by a concrete economic business, which does not necessarily correspond to a significant improvement in patient care. Priorities dictated by science and common sense are not necessarily interesting for Industry. If the scientific community will not be able to modify this tendency, playing a major role in driving this activity, technology improvement will be unpredictable and possibly of little relevance.

In the previous chapter we discussed extensively the current role of robotics in surgery. Today the major perspective and aim is to contribute to simplification of the surgical gesture, in order to increase its reproducibility. This is of course an important advancement, which will possibly offer to a majority of patients the benefits of minimal invasiveness which are now restricted to a minority of patients due to the technical challenges that laparoscopy, at least in some districts, implies. Nevertheless, the benefits of the use of robotics would be even more if we would use this technology to devise less invasive procedures for common diseases, taking advantage of miniaturisation. Applications of a similar technology would be both endoluminal, such as for instance, local excision of large sessile lesions of the digestive tract, overtaking the evident limits of flexible endoscopy compared to surgical platforms (50), and translumenal, such as appendectomies or cholecystectomies, bowel resections and similar procedures.

Against this background, it is realistic that NOTES will not take over endoscopic surgery, and will remain as an application for highly selective procedures. The vast majority of digestive surgery will be most likely performed endoscopically but through the thoracic or abdominal wall, by means of smaller incisions, with the extent of resections reduced either by association with node sampling techniques (51,52), or with biologically tailored therapies. In this perspective it will be mandatory that gastroenterologists and surgeons blend into a new kind of specialist, and perhaps technology development may finally drive them in that direction. Factors that will determine the introduction of new technologies in the clinical armamentarium have to do not only with the value of the technical and clinical improvement, but also with coverage (reimbursement), adoption by practitioners, and competing technologies.

“Inventing the future does not simply require technological innovation but is a complex intellectual exercise that begins with the identification of true unmet needs and profound insight into disease mechanisms” (53)”.

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