



The primacy of embryological, ontogenetic and specimen orientated (mesenteric) surgery as the most important tool in treating visceral (colorectal) cancer

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Abstract: Despite all the molecular markers, pharmaceutical innovations, genetic revolution and scientific advancement, surgery still remains the most effective way to cure visceral cancer. As all members of the Colorectal MDT know, chemotherapy is an *adjunct* to good quality surgery not a replacement, and radiotherapy does not absolve poor quality surgery. Despite this clear truth, most of the money, glamour, RCTs and attention are directed towards medical oncological advances and not surgical ones. Herein the author seeks to outline his reasoning for mesenteric based surgery along embryological, ontogenetic planes as the key factor in governing oncological outcome in the vast majority of cases; outline the fundamental concepts inherited from three surgical doyens, “3 H’s” of surgery—Heald, Holm and Hohenberger, and finally examine some data and reflect on the importance of case selection. This will start with the rectum (following TME principles) and build on from there.

Keywords: Mesentery; TME; complete mesocolic excision (CME); embryology; ontogenetics; colorectal cancer

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Introduction

It is clear from examining the *Lancet Oncology* Commission on Global Cancer Surgery document in 2015 that surgery delivers a dramatic blow to visceral cancer and is a key player on the scene—“Of the 15.2 million cases of cancer in 2015, over 80% of the cases will need surgery, some several times”. Despite this, only 5% of global cancer research is devoted to surgery. It is interesting to postulate the (many) reasons why this may be. Perhaps it’s easier to do trials with drugs and placebos; the fact that surgical technique however standardised may vary and the profound influence of the pharmaceutical industry but to name a few.

Surgery is clearly critical when dealing with cancer at each stage of presentation: curing the disease in early stages, reducing local recurrence, palliating symptoms of advanced disease and prolonging life through metastasectomy.

Looking back at the advances of surgical evolution one thing stands tall as a pillar of achievement—mesenteric

planar based surgery.

Prior to formal mesenteric based surgery, the fundamental principle of cancer surgery (which in principle remain, but have been refined somewhat) is that of complete tumour removal with associated lymphatics and blood vessels.

The need for wide margins and a quick and aggressive resection remained the foundations of surgeons of the past. There was acceptance of collateral damage as almost an inevitable necessity—the late and great John Golligher is said to have quoted something along the lines of “if you’ve not made the patient impotent by the end of the operation, you’ve probably not cured him of rectal cancer”. This idea has evolved with time as can be seen by the rapid evolution in surgery for breast cancer, beginning with the radical Patey mastectomy to much more limited resections (somewhat differently due to multimodality therapy rather than adoption of an anatomical approach).

This view has been refined due to a clearer understanding

of the anatomy, embryology and the recognition that cancer generally tends to remain confined to one embryological compartment (ontogenetic theory).

To my mind, mesenteric based surgery and its power for the good of the patient and satisfaction for the surgeon can be summed up by marrying two concepts. The first is what the great Bill Heald (RJ Heald) of Basingstoke, the father of TME surgery, stated in his seminal paper in 1988, “surgery is a craft... and it is an artisan’s pleasure in the actual style of performing an operation”. Marrying this technical endeavour with the take home message from the English National Low Rectal Cancer Programme of “Decisions are more important than incisions” to me summarises the essence of mesenteric based surgery. The knowledge and joy of dissecting in precise embryological planes in *carefully selected* cases is the recipe for success in cancer surgery and also makes the whole exercise an enjoyable one for the surgeon.

Although there have been many references to mesenteric based surgery throughout surgical history, it was really the popularization of this concept by Bill Heald in the late 1970s and early 1980s that gave it momentum. At that time the local recurrence rate for rectal cancer averaged between (a staggering) 25–35%. Undoubtedly this was predominantly down to technique—the blunt dissection of the rectum with a hand in the pelvis (producing a characteristic “squelching” noise) would result in a shredded mesorectum, significant blood loss for the patient and due to clamping and ligating the “lateral ligament” impotence for the patient with destruction of the nerves of “pelvic happiness”. Bill Heald taught us that if we are patient and thoughtful we can in fact identify embryological planes in the pelvis, and that the endeavour need not be one of haste and roughness but rather precise sharp dissection.

He emphasized that the secret of successful surgery was in finding and following these planes, developed through traction and counter-traction—the reward would be loose areolar tissue (“cheveux d’ange, angels hair) that would invite you to continue further in that plane. The key concepts of the midline gut and its mesentery being covered by visceral fascia and the retroperitoneum and parities being lined by parietal fascia and that the dissection plane between them, identified through traction and counter-traction was “holy”. This was rewarded with an impressive low, single digit local recurrence rate and subsequently improved survival. It was not only an effective cure for cancer which had reduced the need for radiotherapy but also an optimal way of respecting and preserving structures

that did not need to be sacrificed such as the autonomic nerves. Resection of nerves (unless directly involved by cancer) adds nothing to improved cancer outcome and yet does add to the misery of the patient with subsequent bowel, bladder and sexual dysfunction.

These anatomical truths became very clear to surgeons despite the anatomists being slow to take them on board.

During this time whilst the outcome for rectal cancer through anterior resection was improving, the outcome for low rectal cancer and abdominoperineal excision was noted to be particularly poor across all groups, throughout the country and world for that matter. An increased circumferential margin positivity rate and tumour perforation resulted in the development of the “extralevator abdominoperineal excision of the rectum” (ELAPE) approach. Again an important exercise in achieving an R0 resection but modifying the plane of dissection to one outside the levators to avoid wasting of the specimen that would result from following the TME Holy plane down to pelvic floor from above.

Cue Werner Hohenberger who published his paper in 2009 showing both a reduced local recurrence rate and also an improved survival if one follows holy embryological planes in colon cancer surgery through a “complete mesocolic excision” (CME) combined with “central vascular ligation” (CVL).

These concepts fall in line with the ontogenetic theory of local tumour spread. This claims that local dissemination is facilitated in the ontogenetic compartment of origin, yet suppressed at its borders in the early stages of cancer development. As clinicians we often recognize this—it is very rare for rectal cancer to penetrate Denonvilliers septum/fascia however often we suspect it. It seems that in the midst of chaos and haphazard cell growth, ironically there remains some order. Proponents claim that optimal local control of cancer is achieved by whole compartment resection with intact margins following ontogenetic planes.

Despite initial scepticism from surgeons with regards to TME—the time required and the impressively low local recurrence rates, cumulative data from multiple centres in the UK and Europe gradually convinced the surgical community that this was an effective treatment. This process somewhat echoes Schopenhauer’s stages of change: first ridiculed, second violently opposed and finally accepted as self-evident.

In terms of data supporting mesenteric based surgery, the Basingstoke data (1-4) validated by outsiders is very strong (John MacFarlane was a Canadian Professor of

Surgery from Vancouver). Later, trials coming out of Europe (5) and Worldwide (6) have confirmed the importance of the plane of resection as a governing factor in outcome. Werner Hohenberger's data has shown a difference in both local recurrence and overall survival—6.5% to 3.6% local recurrence with CME and increase from 82% to 89% 5-year survival (7). Interestingly the reduction in local recurrence is not as dramatic as in anterior resection and it may be because surgeons were always less likely to be rough and bluntly dissect the abdominal colon rather than the more fixed pelvic rectum.

The above highlights the power of surgery in the vast majority of cases where cancer is non-metastatic and confined to the specific compartment of origin.

In (rarer) cases that permeate through these planes, the key point is early diagnosis. Early recognition with radiology (and occasional clinical suspicion from examination, though probably considered somewhat old fashioned now) allows targeted decision making. This may be (commonly) in the form of neoadjuvant chemoradiotherapy for rectal cancer; en bloc resection or even cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). A detailed understanding of the local cancer spread allows one to plan surgery with the use of other tools and also to stratify the patients risk of local recurrence among other parameters (classic example from the MERCURY (8) trial of classification into “good, bad and ugly”).

It is noteworthy that when discussing success of cancer treatment it is really the fundamental principles of what a resection seeks to achieve rather than the access technique through which it is performed. Open, laparoscopic, transanal and robotic are just different ways of performing the same mesenteric based, embryological, ontogenetic resection. It is the quality of the specimen as judged by the pathologist which governs local cure and overall survival and not the way it was removed. The access technique undoubtedly add many other bonuses in terms of length of stay, cosmesis, hernia incidence, access to the narrow male pelvis as well as potentially better and more precise preservation of structures. What can be resected remains much the same across the board, yet what remains in the patient *may* vary with the access technique, yet there are no trials currently that show this.

Conclusions

Whatever way it is done, it is the precise dissection, in clear embryological planes in correctly selected patients that will

give both the best oncological outcome and (hopefully) the best quality of life for the patient.

It seems therefore when considering advances in cancer surgery that we have answered the question of cure in visceral cancer. It is down to mesenteric based, embryological, ontogenetic, specimen orientated surgery. That is the answer, and it seems all that remains, are more and more precise ways of doing it, though a less and less invasive approach.

I would advocate caution in this view that we have reached the intellectual apex. Looking back in history, this has happened before...

“There is nothing new to be discovered in physics now... all that remains is more and more precise measurement” Lord Kelvin, 1900.

This bold statement was 5 years before Albert Einstein published his Nobel prize winning paper on the photoelectric effect (though awarded it some years later) and before all the advances in quantum mechanics that we take for granted today. Whilst we have undoubtedly achieved an awful lot in surgery, there will always be room for more and an open mind remains necessary.

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None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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