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ANATOMICAL CONSIDERATIONS FOR THE IMPROVEMENT OF SIDE EFFECTS OF RADICAL PROSTATECTOMY: THE INFLUENCE OF ROBOTIC SURGERY

Introduction

Despite good results regarding oncologic outcomes, well-known adverse events follow radical prostatectomy; including incontinence and erectile dysfunction. The first revolution came in the 1980's from the work of Walsh and Donker; aided by laboratory dissections, a systematic operation was described in order to provide adequate cancer control, in addition to preserving continence and erectile function. The 2000's have seen another revolution in the form of the introduction of robotic radical prostatectomy[1, 2]. Urinary incontinence is, by far, the most feared side effect by the patient being a major cause of distress, social withdrawal, increased psychological and the financial burden of pads, this also includes secondary procedures such as urethral slings, urethral bulking procedures and artificial sphincter implants [21]. These side effects often impact the choice of treatment. Immediate and short term results of urinary control at catheter removal, first, second, and third months after surgery range from (0 – 80%), (22 – 80%), and (40 - 90%) respectively, these results leave a lot to be desired [22, 23, 24, 25, 26, 27, 28]. With improved oncologic outcomes, urologists and their patients are becoming increasingly ambitious regarding functional outcomes and quality of life, leading to the development of the

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concept of a “Trifecta” of oncologic control, recovery of urinary control, and potency [29, 30].

Principles of surgical anatomy

Understanding the principles of surgical anatomy is the first key step to any successful surgery. More than a century has passed since the first radical prostatectomy by Hugh Young, and, yet, several uncertainties still exist as to which surgical technique offers the best immediate functional outcome, while also respecting the oncologic principles. As mentioned in the seminal article by Koraitem, the structural plan of the human body is characterized by a “*duplication of safety mechanisms to maintain function*” [3]. The etiology of post prostatectomy incontinence (PPI) is multifactorial; consisting of non-modifiable variables, including advanced age, obesity, pre-operative incontinence, short urethral length, detrusor instability, prostate volume, and disruption of normal anatomy [4, 5]. Modifiable variables include surgeon/institution volume [6], preservation of urethral sphincter [7], and presservation of suspensory anatomical support [8].

Urethral sphincter complex

The external urethral sphincter complex is considered by the majority of authors to be the most important structure contributing to the maintenance of post-operative continence. According to Dorschner and Stolzenburg, the distal urethral sphincter is composed of an outer striated and inner smooth muscle component. The smooth muscular part of the external sphincter, “lissosphincter”, is the most likely structure to ensure continence at rest after resection of the internal vesical sphincter following radical prostatectomy or transurethral resection (TURP) [9]. Under normal conditions, urine is stopped at the level of the vesical orifice, after TURP it arrests at the distal limit of the prostatic cavity where the lissosphincter is intact. Following prostatectomy, a variable portion of lissosphincter is resected. This might contribute to post-prostatectomy incontinence. The striated component exerts its function from the prostate apex to the penile bulb, whereas the inner smooth muscle component extends at least to the verumontanum [10]. In some studies, the striated portion was shown to contain both “fast twitch” and “slow twitch” fibers; the fatigue-resistant slow twitch fibers being partially responsible for sustained continence at rest, and fast twitch fibers contributing to continence during periods of sudden increase in intra-abdominal pressure [11]. As mentioned previously, **apical configuration** is another challenge which confronts the surgeon attempting to preserve as much urethral length while also avoiding a positive urethral margin. Lee and colleagues have shown that the prostatic apex overlaps with the striated sphincter anteriorly, posteriorly, bilaterally or unilaterally in 85% of their patients [12]. These facts mandate precise dissection of the apex in order to avoid inadvertent resection of valuable functional urethral tissue. In addition to urethral length, urethral integrity is also an important determinant of recovery of continence. The striated sphincter is related anteriorly to the dorsal venous complex which may invaginate the sphincter’s anterior portion [13]. Theoretically, this fact makes the muscle fibers of the striated sphincter vulnerable to entrapment by the standard DVC stitch, which was illustrated in an anatomic study by Ganzer and colleagues [14]. According to many authors, apical dissection is arguably the most important technical predictor of recovery of continence after radical prostatectomy [15], unfortunately it is surgeon dependent and is difficult to measure objectively.

Neurovascular bundle (NVB) sparing

The pelvic plexus is the central neural plexus that provides autonomic innervation to male urogenital organs. Dissection and preservation, whenever possible, of the cavernous nerves that run from the NVB to the cavernosal bodies during radical prostatectomy are essential to preserve erectile function. This is an especially challenging task considering that the arrangement of these nerves is characterized by marked anatomic variabilities [16]. Contemporary studies on adult specimens describe the neural structures as widely dispersed along the anterolateral, lateral, and posterolateral aspect of the prostate [16, 17], as opposed to the classic “localized posterolateral bundle” description in fetal dissections [18]. Nerve-sparing surgery allows for a better chance at preserving potency [5]. Also, of note is that some anatomic studies have shown that the neurovascular bundle provides at least some neural contribution to the membranous urethra [19, 20]. Cadaveric dissections demonstrated that the sympathetic nerves from sacral segments S2 to S4 provide autonomic supply to the smooth muscle sphincter of the membranous urethra, and the somatic nervous branches from the pudendal nerve innervate the striated urethral sphincter [21]. This anatomic hypothesis was associated with a faster return of continence in a number of clinical studies [22, 23, 24].

Supporting anatomy

The prostate is attached anteriorly and antero-laterally to the pubic bone with the puboprostatic/pubovesical ligaments. These ligaments are paired fibrous bands; they appear in the sagittal plane as a triangular fascial structure that attaches the pubic bone to the fascia of the striated sphincter, anterior surface of the prostate and the urinary bladder [25]. The ligaments then blend laterally with a fibrous thickening of the endopelvic fascia "arcus tendinous fascia pelvis"; representing a tough structure that is used in urethral suspension procedures for stress urinary incontinence [26]. Together with the puboperinealis portion of the levator ani muscle the ligaments and the arcus tendinous fascia form the "puboprostatic collar" which is believed to provide important structural support to the urethra and maintain urinary control.

The previously mentioned anatomic facts have prompted many surgeons to experiment with a variety of reconstruction techniques including; anterior suspension stitch, pubourethral ligament sparing, puboprostatic collar sparing, posterior reconstruction of the musculo-fascial plate [27, 28, 29], and Retzius-sparing prostatectomy [30, 31].

Influence of robotic surgery

One can argue against the superiority of robotic prostatectomy, compared to open and laparoscopic approaches, since level I evidence is still lacking. However, it is difficult to disagree that since the introduction of the robot, many new research avenues have been opened. A PubMed search (keywords; prostatectomy, robotic prostatectomy) indicates that the number of publications has substantially increased (**Figure 1, Figure 2**). Since the introduction of robotic prostatectomy in the year 2000, a surge of new techniques regarding radical prostatectomy have been introduced to the literature, possibly due to the fact that a robot provides the surgeon with the ergonomics to dissect exactly how and where he wants to.

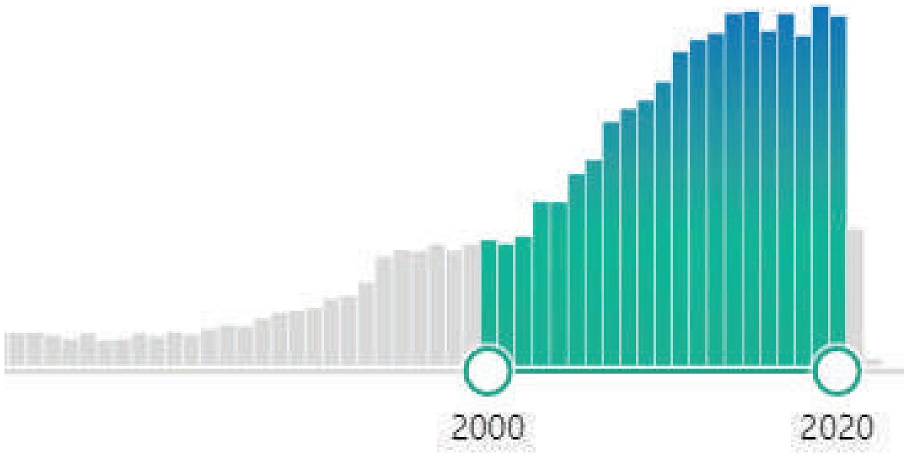

Figure 1 – Pubmed search results for "Prostatectomy"

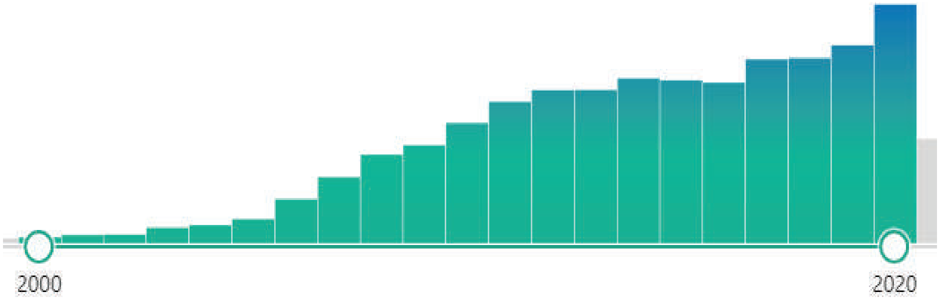

Figure 2 – Pubmed search results for "Robotic Prostatectomy"

Robotic surgery has offered the minimally invasive advantages of laparoscopy, with the added benefits of stereoscopic vision, 10-15 times magnification, wristed instruments enabling precise dissection and complex reconstruction. In other words, robotic surgery was designed to overcome the shortcomings of conventional laparoscopy and potentially reduce the learning curve of complex minimally invasive surgery [32].

Some of the techniques described (i.e. puboprostatic collar sparing approach, total anatomical reconstruction, Retzius-sparing) are difficult to perform using traditional laparoscopy, or even open surgery. Pneumoperitoneum allows for better vision due to the tamponade of small venous bleeding. Enhanced optical magnification has provided potentially better identification of anatomic details. Video recording in robotic surgery facilitates with the teaching of early career surgeons.

Due to its prohibitive cost, the robot must clearly demonstrate superiority when compared to open retropubic, and laparoscopic assisted radical prostatectomy.

Table 1, summarizes the data of the most relevant studies. And despite the fact that many studies were characterized by heterogeneous data, small numbers and non-randomized nature/low methodological level, higher quality studies are being observed in more recent publications. A trend towards earlier continence recovery, better potency, lower blood loss and rates of transfusion is being consistently observed with the robot. The results of this data suggest that robotic assisted radical prostatectomy is at least equivalent to other approaches.

The only randomized study which has compared robotic to open prostatectomy has shown equivalence of functional outcomes, and superior outcomes of the robot in terms of intra-operative complications, blood loss and hospital stay. The robotic arm was operated by a fellowship-trained surgeon, having performed 200 robotic cases, compared to an experienced open surgeon with more than 1500 completed cases. If the robot allows a young surgeon to achieve equivalent outcomes to an experienced open surgeon in a short period of time, then this reduction in the learning curve should be considered an advantage [43].

Table 1

Robot compared to open retropubic and laparoscopic assisted radical prostatectomy: The most relevant studies (Modified from Abbou & Abdelbary **Error! Bookmark not defined.**)

Author	Study design	Continence	Potency	Other
Huang et al., 2017 [33]	**Meta-analysis** 24 studies (2 RCT) (9178 patients) (LRP vs. RARP)	Better with RARP	Better with RARP	-Less transfusion with RARP -Similar BCR rate -Similar complication rate
Tang et al., 2017 [34]	**Meta-analysis** No RCTs (Open vs. RARP)	No difference	Better with RARP	-Less transfusion with RARP -Less complications with RARP -Less +ve margins with RARP
Seo et al., 2016 [35]	**Meta-analysis** No RCTs (Open vs. RARP)	Better with RARP	Better with RARP	-Less transfusion with RARP -Similar BCR rate -Less complications with RARP
Moran et al., 2013 [36]	**Meta-analysis** 51 studies (1 RCT) (Open vs. LRP vs. RARP)	Better with RARP (in comparison to open)	Better with RARP (in comparison to open)	-Less complications, LOS with RARP -Less +ve margins with RARP
Ficarra et al., 2012 [8]	**Meta-analysis** (Open vs. LRP vs. RARP)	Better with RARP	Better with RARP	-Less blood transfusion with RARP -Less surgery for incontinence with RARP
Robertson et al., 2013 [37]	**Meta-analysis** (LRP vs. RARP)	No difference	NR	-Less +ve margin with RARP -Less organ injury with RARP

Yaxley et al., 2016 [38]	**RCT** (163 vs. 163 patients) (Open vs. RARP)	No difference	No difference	-Less hospital stay with RARP -Lower blood loss -Similar +ve margin rate
Porpiglia et al., 2013 [39]	**RCT** (60 vs. 60 patients) (LRP vs. RARP)	Better with RARP	Better with RARP	-Similar margin rates -Similar blood loss
Ong et al., 2016 [40]	**Prospective, comparative** (1117 vs. 885 patients) (Open vs. RARP)	Better at 1 year with RARP Similar at 2 years	No difference	-Less +ve margins with RARP -Less BCR with RARP
Haglind et al., 2015 [1]	**Prospective, comparative** (778 vs. 1847 patients) (Open vs. RARP)	No difference	Marginally better with RARP	-Similar margin rates
Beauval et al., 2015 [42]	**Prospective, comparative** (129 vs. 175 patients) (Open vs. RARP)	No difference	Better with RARP	-------
Jackson et al., 2016 [43]	**Prospective, Retrospective comparison** (Early RARP experience vs. Experienced open)	No difference	No difference	-Shorter LOS with RARP -Longer OR time with RARP -Similar +ve margin rate
Jeong et al., 2014 [44]	**Retrospective** (Open vs. RARP)	Better with RARP	NR	
O'Neil et al., 2016 [45]	**Retrospective** (Open vs. RARP)	Better at 6 months with RARP	Better with RARP	
Du et al., 2018	**Meta-analysis** (Open vs. LRP vs. RARP)	Better with RARP	Better with RARP	-Less blood loss -Less +ve margins

➢ “Veil” technique

The “Veil” technique was described by Menon and colleagues [46]. Their first publication reported a 96% potency rate at one year, which was higher than most contemporary series. In this technique, the prostatic fascia is lifted off the prostate without incising the endopelvic fascia or ligating the Santorini plexus. This helps achieve two goals: minimizing traction on the neurovascular bundle, as well as preserving the integrity of the distal sphincter complex by avoiding mass ligation stitch. While this technique has been described later in open surgery [47], it was not used in robotic assisted radical prostatectomy until it was innovated, and repeatedly tried and tested robotically.

➢ Total anatomical reconstruction after robotic prostatectomy

Radical prostatectomy is an operation of resection and reconstruction. Wu and colleagues have hypothesized that posterior reconstruction of the musculofascial plate by suturing the DF to the median dorsal raphe, followed by the vesico-urethral anastomosis and reconstruction of the detrusor apron and the puboprostatic ligaments, could contribute to urethral stabilization and accelerated recovery of continence [48]. This complex reconstruction requires superior ergonomics which is facilitated by the endowrist technology provided by the robotic system.

➢ Lateral approach

Following the concept of zealous preservation of peri-prostatic tissues, Gaston’s group described a technique which allows the prostate to be dissected from the surrounding fascial envelope. Their robotic exposure involves the incision of the fascia lateral to the prostate, thus leaving the rest of the endopelvic fascia and detrusor apron undisturbed**Error! Bookmark not defined.**, effectively following the same principles of the popular “Retzius sparing approach” which is described later. Although technically demanding, they reported a remarkable 80% pad-free rate at catheter removal in their cohort of 30 patients. Despite the small sample size of the study, and the cohort being comprised of relatively young patients, the results were encouraging.

- **Retzius sparing prostatectomy**

Described by Galfano and colleagues [29], the concept of Retzius-sparing approach aims to minimize dissection around the prostate. Recent reports have elucidated the importance of the suspensory structures of the pelvis surrounding the prostate in maintaining post-prostatectomy urinary control. In addition, the approach theoretically maximizes sparing the periprostatic fascia including the neural structures contributing to potency. Dissection involves working in the field of exposure which is very limited and is extremely difficult to implement in open surgery. The inherent advantages of the robot include; 7 degrees of freedom, high fidelity magnification as well as camera access to the depth of the pelvis, thus allowing the surgeon to execute these demanding surgical maneuvers efficiently.

- **Perineal prostatectomy**

The first attempt at robotic perineal prostatectomy on a cadaver was performed by the Cleveland Clinic group [49]. The procedure was performed on patients in 2019 [50]. While the number of cases performed is still too small to draw any comparative conclusions with the traditional approach, robotic perineal prostatectomy was found to be feasible and safe. In addition, it has the potential advantages of avoiding an abdominal incision and intraperitoneal adhesions, and better access to the prostate in obese patients [51]. Limiting factors to this approach can be dissection of large prostates, and the requirement of an Xi or Single port robot in order to perform with less difficulty.

- **Single port prostatectomy**

The Da Vinci single port (SP) preclinical model was purposefully designed to accommodate the robotic camera and instruments, to tackle confined spaces through a single incision. The authors demonstrated the feasibility of robotic SP transabdominal prostatectomy, perineal prostatectomy as well as robotic pelvic lymphadenectomy from the perineal approach [52, 53]. The introduction of the new machine opens new frontiers for robotic surgery, but also raises some controversy regarding the limited working space, instrument clashing and longer operative time. It also requires a highly experienced operator and a skilled assistant [54]. It is argued that the single port robot opposes the intuitive concept of robotic surgery which is designed to reduce complexity rather than increase it.

- **Robotic surgery for benign disease of the prostate**

The standard treatment for benign prostatic hypertrophy for huge (>80 gm) prostates has been open transvesical or retropubic prostatectomy. Robotic simple prostatectomy offers the advantages of being less invasive than its open counterpart, is relatively easy to perform for an operator with experience in robotic urologic surgery, lower risk of urethral injury, and is associated with a less step learning curve when compared to new effective modalities such as HoLeP (Holmium laser enucleation of the prostate) [55]. A reported advantage for robotic simple prostatectomy over HoLeP is the lower risk of urine incontinence (4.6 – 22%) [56].

- **Application of new technologies in robotic prostatectomy**

Improving surgical outcomes is another dynamic goal for which urologists continuously strive to achieve. One component of improving surgical outcomes is enhancing the level of training which the novice surgeon receives. The “Agency for healthcare research and quality”, estimated the annual cost to US healthcare from medical errors is €17.1 billion, a large proportion of which were believed to be avoidable [57]. Consistent video recording in robotic surgery has provided opportunities to assess performance and competence with an unprecedented zeal, so much so, that some authors have ambitiously envisioned computer-based assessment using machine learning [58, 59, 60, 61].

Another technology which has seen integration in robotic surgery is the combined use of near-infrared fluorescence (NIRF) and Indocyanine green (ICG); which enables the enhancement of anatomy and the mapping of relevant vasculature. This technology has seen some promising applications in robot-assisted partial nephrectomy; especially in identifying suitable tissue for resection included within the ischemic area of the kidney, and allowing super-elective vascular identification and clamping. It also aids in guiding tumor resection with an appropriate safety margin. NIRF + ICG has also been investigated as a way to enhance the delineation of the neurovascular bundle during nerve-sparing surgery.[62] In robotic radical prostatectomy, the technology has been tested to guide lymph node dissection, and has demonstrated a potential to identify sentinel lymph nodes after coupling ICG to nanocolloid [63]. However, that feasibility was not replicated by Chennamsetty and colleagues, and they concluded that ICG guided lymph node dissection cannot replace established lymph node dissection [64].

Machine learning and artificial neural networking can also be applied in other domains; one study evaluated the use of artificial intelligence to predict recovery of urinary control using automated performance metrics, and reported 85.9% accuracy in this prediction [65]. Other investigators have explored the application of augmented reality 3D imaging during robotic surgery; one group has devised a technique to superimpose a real-time image of the prostate neoplasm based on pre-operative MRI findings and intraoperative transrectal ultrasound during robotic prostatectomy [66]. In their study, Porpiglia and colleagues have reported that using a 3D model to guide resection during robotic prostatectomy has led to a reduction of positive surgical margin rates in pT3 disease (5.7% in the 3D group versus 26.7% in the control group, $p < 0.05$) [67]. Another study used a tablet computer to provide real time mapping to aid in identification and preservation of important anatomical structures during RARP in four patients [68].

While this effort is still in its infancy, it can be a source of limitless applications. One can only wonder if these applications can lead to a fully automated prostate cancer operation in the not too distant future.

Conclusion

It is evident from the trend of publications during the last two decades that robotic surgery will continue to expand and further evolve. Regarding prostatectomy, the robotic interface has popularized prostate cancer surgery across the globe. It did not compromise oncologic control, but brought forward important advantages as reduced blood loss, early recovery and a trend towards better urinary and erectile function. The technology allowed the urologists and their patients to become more ambitious regarding functional outcome; the procedure now focuses on preserving quality of life as much as ablating the cancer. Moreover, there has been an evident increase in academic competition in devising new techniques to achieve these goals. From a broader point of view, robotic surgery has the potential to become integrated with various artificial intelligence tools, allowing for unprecedented efficiency and autonomous decision making.

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