CUAJ – Review Al-Jabir et al

Review: Status of wet lab and cadaveric simulation in urological training

# Current status of wet lab and cadaveric simulation in urological training: A systematic review

Ahmed Al-Jabir<sup>1</sup>; Abdullatif Aydın<sup>2</sup>; Hussain Al-Jabir<sup>3</sup>; M. Shamim Khan<sup>2,4</sup>; Prokar Dasgupta<sup>2,4</sup>; Kamran Ahmed<sup>2,5</sup>

<sup>1</sup>GKT School of Medical Education, King's College London, London, United Kingdom; <sup>2</sup>MRC Centre for Transplantation, Guy's Hospital, King's College London, London, United Kingdom; <sup>3</sup>William Harvey Research Institute, Barts and The London School of Medicine School of Medicine and Dentistry, London, United Kingdom; <sup>4</sup>Department of Urology, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom; <sup>5</sup>Department of Urology, King's College Hospital NHS Foundation Trust, London, United Kingdom

**Cite as:** *Can Urol Assoc J* 2020 June 5; Epub ahead of print. http://dx.doi.org/10.5489/cuaj.6520

Published online June 5, 2020

\*\*\*

#### **Abstract**

**Introduction:** We undertook a systematic review of the use of wet lab (animal and cadaveric) simulation models in urological training, with an aim to establishing a level of evidence (LoE) for studies and level of recommendation (LoR) for models, as well as evaluating types of validation.

**Methods:** Medline, EMBASE, and Cochrane databases were searched for English-language studies using search terms including a combination of *surgery*, *surgical training*, and *medical education*. These results were combined with *wet lab*, *animal model*, *cadaveric*, and *in-vivo*. Studies were then assigned a LoE and LoR if appropriate as per the education-modified Oxford Centre for Evidence-Based Medicine classification.

**Results:** A total of 43 articles met the inclusion criteria. There was a mean of 23.1 (±19.2) participants per study with a median of 20. Overall, the studies were largely of low quality, with 90.7% of studies being lower than 2a LoE (n=26 for LoE 2b and n=13 for LoE 3). The majority (72.1%, n=31) of studies were in animal models and 27.9% (n=12) were in cadaveric models.

**Conclusions:** Simulation in urological education is becoming more prevalent in the literature, however, there is a focus on animal rather than cadaveric simulation, possibly due to cost and ethical considerations. Studies are also predominately of a low LoE; more higher LoEs, especially randomized controlled studies, are needed.

#### Introduction

The Halsteadian model of 'see one, do one, teach one' has long permeated and monopolised surgical education<sup>1</sup> with surgeons learning surgical techniques in an 'apprenticeship' style under an experienced surgeon in the OR. However, in modern medical practice, service delivery pressures have reduced training hours and so new ways must be found to enhance and be an adjunct to patient and operation exposure hours.

The solution of the aviation industry has long been to use simulation models to enhance learning<sup>2,3</sup> and this style of learning is also becoming more widely adopted and validated as a way to enhance performance in the operating room (OR) in a surgical setting <sup>4-7</sup>.

Despite the widespread use of bench-top dry lab models, the gold standard of simulation-based surgical training is still using wet lab models, consisting of animal models (both live animals and animal tissues) and cadaveric simulation models. The advantages and disadvantages of these are summarized in Table 1.

Previous systematic reviews have been published on the use of surgical simulators in specific specialities<sup>8-12</sup> but to date, none have comprehensively focused on the use of wet lab simulation models, especially in urology.

The aim of this study is to systematically review the literature base for the use of wet lab simulator models in urological surgery, to establish a level of evidence (LoE) for studies, a level of recommendation (LoR) for models, as well as evaluating types of validation used in studies.

#### Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to optimise the transparency and detail of the review <sup>13</sup>

#### Eligibility criteria

Included in the review are original research articles and systematic reviews, as well as posters and oral presentations from conferences that described the use of wet lab models for surgical simulation. Studies included were those that were validation studies or articles studying the educational value of a model. Systematic reviews, insufficiently short abstracts and articles not in the English language were excluded as well as those relating specifically to dental surgery.

# Information sources and search processes

Studies were identified by searching MEDLINE, EMBASE and Cochrane Library databases via Ovid from 1946 to present using the strategy in Supplementary Data 1. Search terms included a combination of *surgery*, *surgical training* and *medical education*. These results were combined with *wet lab*, *animal model*, *cadaveric* and *in vivo*.

## Study selection and data collection process

After the initial search, abstracts and titles were screened as well as duplicates removed. Articles chosen were agreed upon by all authors. Full texts were then reviewed to exclude non-urological articles as well as those that do not meet the inclusion criteria. Further to this, a hand search of reference lists was done for any further articles missed.

#### Data items

Data extracted was as follows: Author; Year; Type of simulation model; if animal model, which animal; if animal model, whether in-vivo or ex-vivo; Procedure simulation method tested for; Subjects size; Validation type; Brief description; Level of recommendation; level of evidence (if appropriate)

Each study was classified for validity where appropriate using the definitions developed by McDougall <sup>1</sup>, Van Nortwick, Lendvay, Jensen, Wright, Horvath, Kim <sup>14</sup> and Tay, Khajuria, Gupte <sup>15</sup> (See Supplementary table 1).

A level of evidence (LoE) and Level of recommendation (LoR) was given to each study and model as according to the modified educational Oxford Centre for Evidence-Based Medicine classification system, as adapted by the European Association of Endoscopic Surgery <sup>16</sup> (See Supplementary tables 2A-2B)

## Synthesis of the data

Due to the heterogenous and qualitative nature of many of the studies, a quantitative metaanalysis could not be performed.

#### **Results**

## Description of included studies

A total of 498 studies were identified for potential inclusion. After screening of abstracts and full text review, 143 articles met criteria for inclusion in the study. Of the 140 articles included, 43 studies were identified as dealing with urological procedures<sup>17-58</sup>.

There were a far-ranging number of participants of each study, ranging from 2-102 with a mean of 23.1 ( $\pm$  19.2), a median of 20 participants and a mode of 20 participants per study. Overall, the studies were largely of low quality with 90.7% of studies being lower than 2a Level of Evidence (n=26 for LoE 2b and n=13 for LoE 3). Subsequently, they had low levels of recommendation (58.5% LoR 3, 31.7% LoR 4).72.1 % (n=31) of studies were in animal models and 27.9 % (n=12) were in cadaveric models. 27.9% (n=12) were cadaveric studies, 26 studies were porcine studies and 4 were chicken studies (see Table 3). 31.7% of studies (n=13) were descriptive-only studies with the others involving elements of evaluation. For evaluation studies, the average number of participants was 23.6 ( $\pm$  20.7) with a median of 20. 18 studies had elements of content validity evaluation and 17 studies examined construct validity. 58.3% of cadaveric studies had a LoE of 2b with the rest having a LoR of 3. Of animal studies, 3 studies demonstrated a LoE of 2a, 61.3% (n=19) had a LoE of 2b and 9 studies were descriptive-only studies with a LoR of 4.

CUAJ – Review Al-Jabir et al

# Review: Status of wet lab and cadaveric simulation in urological training

The studies described a wide variety of simulation models covering percutaneous nephrolithotomy, flexible and semi-rigid ureterenoscopy as well as nephrectomy simulation models.

#### Laparoscopic surgery

Eight studies were identified for the simulation of laparoscopic procedures

#### Nephrectomy

Molinas <sup>44</sup> trained 10 medical students and 10 specialists in laparoscopic nephrectomy on a live rabbit model finding a reduction in operative time as well as significant differences between the experienced and novice groups.

6 moderately-experienced laparoscopic surgeons were trained in radical nephrectomy on a live porcine model by Cruz, Passerotti, Frati, Reis, Okano, Gouveia, Biolo, Duarte, Nguyen, Srougi <sup>26</sup>. They found reduced blood loss, increased depth perception and dexterity from the initial training session showing face and content validity.

De Win, Van Bruwaene, Allen, De Ridder <sup>56</sup> designed a model with a porcine kidney which is connected to a pulsatile pump and participants (n=22) were instructed to dissect the renal vessels, finding construct validity.

A study by Marchini, Fioravanti, Horta, Torricelli, Mitre, Arap <sup>43</sup> enrolled 15 urologists in a course to learn single incision laparoscopic total nephrectomy in a live porcine model and demonstrated face and content validity.

#### *Pyeloplasty*

Ramachandran, Kurien, Patil, Symons, Ganpule, Muthu, Desai <sup>59</sup> developed a chicken-crop and oesophagus model to simulate laparoscopic pyeloplasty. Following from this study, Jiang, Liu, Chen, Wang, Lin, Xu, Han, Huang, Huang <sup>17</sup> demonstrated the construct validity of this model with 15 participants of varied experience.

Teber, Guven, Yaycioglu, Ugurlu, Sanli, Gozen, Rassweiler <sup>24</sup> describe a one-knot pyeloplasty model using a porcine bladder with 5 laparoscopic surgeons finding a 21% reduction in anastomotic time after training showing construct validity.

#### Urethrovesical anastomosis

Four studies used chickens to simulate urethrovesical anastomosis. Yang, Bellman <sup>18</sup> used chicken skin folded on a catheter to simulate a bladder and urethral stump (n=8) with Laguna, Arce-Alcazar, Mochtar, Velthoven, Peltier, de la Rosette <sup>19</sup> using the oesophago-glandular-stomach junction of chicken carcasses (n=5) and Boon, Salas, Avila, Boone, Lipshultz, Link <sup>27</sup> using a section of pig intestine (n=12). All models demonstrated construct B validity.

Sabbagh, Chatterjee, Chawla, Hoogenes, Kapoor, Matsumoto <sup>28</sup> evaluated a model using live anaesthetised pigs with an RCT comparing the model with a foam pad bench-top model and the group trained on the simulator outperformed the control group, also demonstrating face validity.

# Endourology

# *Urethrocystoscopy*

Grimsby, Andrews, Castle, Wolter, Patel, Humphreys <sup>38</sup> describe the evaluation of a boar bladder and urethra model by 2 residents for cystoscopy and bladder biopsy. They found an improvement after training with the model and thus demonstrated construct A validity.

Soria, Morcillo, Serrano, Cansino, Rioja, Fernandez, de la Cruz, Van Cleynenbreugel, Sanchez-Margallo <sup>22</sup> describe a live porcine module for Urethrocystoscopy featuring Ureteral orifices cannulation and subsequent ureteroscopy

Bowling, Greer, Bryant, Gleason, Szychowski, Varner, Holley, Richter <sup>55</sup> did an RCT comparing use of fresh-frozen cadavers and a bench-top model for rigid urethrocystoscopy in 29 obstetric residents and demonstrated construct B validity. Additionally, rigid and flexible urethrocystoscopy were two of the modules in the BAUS cadaveric course described by Ahmed, Aydin, Dasgupta, Khan, McCabe.<sup>54</sup>

# Ureterorenoscopy (URS)

20 fully qualified urologists were trained in flexible ureteroscopy by Hu, Liu, Wang <sup>23</sup> using in vitro porcine kidneys and ureters. They found that the average operative time improved by 39% as well as improvement on a global rating scale. Additionally, the authors found that a learning curve was established, plateauing at 6 training sessions.

16 first year medical students trained on a bench-top model or the UROMentor VR simulator in a study by Chou, Abdelshehid, Clayman, McDougall <sup>57</sup> then later independently performed URS on an ex-vivo porcine kidney/ureter model. Both groups performed equally as well proving the concurrent validity of the animal model.

Ogan, Jacomides, Shulman, Roehrborn, Cadeddu, Pearle <sup>58</sup> evaluated 16 medical students and 16 residents on a virtual reality model and then followed it by a diagnostic ureteroscopy on a cadaveric model. They found close correlation between VR and cadaveric performance in students but not in residents. Cadaveric simulation showed construct B validity due to its ability to distinguish between training levels.

Mains, Tang, Golabek, Wiatr, Ross, Duncan, Howie, Tait, Chlosta, Kata <sup>51</sup> designed a course using Thiel-embalmed cadavers to train flexible Ureterenoscopy. 5 urological trainees and 3 faculty members demonstrated face and content validity with high level of satisfaction with the realism and quality of the tissue, however noted the difficulties in variations of anatomy between cadavers including tortuous ureters.

Rai, Tang, Healy, Raslan, Somani, Tait, Nabi <sup>52</sup> also utilised Thiel-embalmed cadavers and demonstrated face validity for the technique especially with regards to anatomical and haptic resemblance however it was noted that endoscopic resection.

Soria, Morcillo, Sanz, Budia, Serrano, Sanchez-Margallo <sup>42</sup> performed a study with 40 participants comparing a bench-top model for URS with laser lithotripsy and stone removal on an ex-vivo porcine model followed by live porcine model demonstrating face, content and construct validity.

Huri, Skolarikos, Tatar, Binbay, Sofikerim, Yuruk, Karakan, Sargon, Demiryurek, Miano, Bagcioglu, Ezer, Cracco, Scoffone <sup>48</sup> used both fresh-frozen and soft embalmed

cadavers for training in flexible ureteroscopy in 12 inexperienced urologists demonstrating a 50.6% improvement in mean operative time with no intraoperative injuries as well as feasibility for reuse in further sessions.

# Percutaneous nephrolithotomy (PCNL)

Mishra, Kurien, Ganpule, Muthu, Sabnis, Desai <sup>36</sup> compared 24 experts performing a percutaneous renal puncture in a live porcine model under C-arm guidance and a virtual reality PERC Mentor (Simbionix, Lod, Israel). They demonstrated construct validity by finding superior realism and usefulness ratings in the animal model.

Earp <sup>30</sup> produced a PERC model using an ex-vivo porcine kidney and a plastic catheter fixed to 3cm thick foam to simulate the retroperitoneal tissue. This model was found to be useful as well as cheap and able to be reused however it was not possible to use ultrasound guidance using this model.

Hammond, Ketchum, Schwartz <sup>32</sup> used a model where a porcine kidney with an artificial stone was placed inside a chicken carcass to simulate the layers of human posterior tissue. They demonstrated face validity particularly with regards to percutaneous renal access.

Zhang, Ou, Jia, Gao, Cui, Wu, Wang <sup>35</sup> used porcine kidneys wrapped in a full-thickness skin flap with 42 urologists and assessed face validity finding 85.7% rating it 'helpful' or 'very helpful'.

Hacker, Wendt-Nordahl, Honeck, Michel, Alken, Knoll <sup>31</sup> designed a model modified from that of Hammond, Ketchum, Schwartz <sup>32</sup> using a porcine kidney, a chicken carcass and artificial stones with the addition of a layer of ultrasound gel surrounding the kidney to enable more effective ultrasound monitoring.

Strohmaier, Giese <sup>34</sup> developed a model using a porcine kidney embedded in silicon and filled with stone and demonstrating high ratings for haptic feedback and realism of tissue. This model was later improved in a follow-up study<sup>33</sup> by embedding the model in porcine thoracic/abdominal wall tissue to simulate retroperitoneal tissue in humans.

Jagtap <sup>37</sup> compared a virtual reality PCNL model to simulation in live anaesthetised pigs and found the live porcine model to be superior in realism (4.44/5 vs 2.75) and superior usefulness as an assessment tool (4.68 vs 2.75) however noted that the virtual reality model enabled repeated use and was easier to set up.

Jutzi, Imkamp, Kuczyk, Wolters, Stoehrer, Kruck, Walcher, Nagele, Herrmann <sup>25</sup> followed by Jutzi, Imkamp, Kuczyk, Walcher, Nagele, Herrmann <sup>29</sup> used ex-vivo porcine kidneys placed between two full thickness skin lobes in a laparoscopic trainer with an adjustable plate enabling simulation of prone, upright or supine patient positioning. All participants rating the model useful for training PCNL.

### Robot-assisted surgery

Seven studies were identified for robot-assisted procedures.

#### *Nephrectomy*

Hung, Ng, Patil, Zehnder, Huang, Aron, Gill, Desai <sup>20</sup> described a model for robot-assisted partial nephrectomy using porcine kidney and a Styrofoam ball to a mimic renal tumour in the da Vinci Skills Simulator (dVSS; Intuitive Surgical, Sunnyvale, CA, USA), a simulator version of the most commonly used surgical robot. They established face, content and construct validity in 46 participants, including 28% being experts.

In a follow-up study, Hung, Patil, Zehnder, Cai, Ng, Aron, Gill, Desai <sup>21</sup> established concurrent and predictive validity in 24 participants.

# Renal transplantation

Khanna, Horgan <sup>39</sup> developed a model for robot assisted ex vivo kidney transplantation using porcine kidneys and the dVSS focussing on the skills for venous and arterial anastomoses. The model was assessed by a single specialist robotic surgeon and show improvement in time taken after repeated training with the dVSS as well as reduced leak rates and increase in 'surgical finesse'.

Tiong, Goh, Tan, Chiong, Vathsala <sup>41</sup> used a live porcine model for robot-assisted kidney autotransplantation with a primary outcome of arterial anastomotic time for intermediate transplant surgeons with prior robotic experience, establishing face and content validity. In addition, they used intraoperative indocyanine green imaging was used to test perfusion of the graft.

## Robot-assisted radical prostatectomy

Alemozaffar, Narayanan, Percy, Minnillo, Steinberg, Haleblian, Gautam, Matthes, Wagner <sup>40</sup> established face, content and construct validity in 20 participants for a porcine genitourinary model for robot-assisted radical prostatectomy.

# Training courses

22 residents participated in a robot assisted surgical training course using fresh-frozen cadavers by Blaschko, Brooks, Dhuy, Charest-Shell, Clayman, McDougall <sup>49</sup> in combination with cardiac surgery training with face validation established.

Raison, Ahmed, Aydin, Khan, Dasgupta <sup>50</sup> ran a novel cadaveric training course for radical cystectomy, radical prostatectomy, extended lymph node dissection and radical nephrectomy using fresh-frozen cadavers for 16 delegates using the dVSS finding face, content and construct validity.

Ozcan, Huri, Tatar, Sargon, Karakan, Yagli, Bagcioglu, Larre <sup>53</sup> used cadavers as part of a surgical anatomy training course using theoretical lectures and practical dissection focussing on renal, prostatic, bladder and penile/scrotal anatomy. 50 urological residents undertook the course and their knowledge, as tested by a written multiple-choice examination improved by an statistically significant 11.1%.

Al-Jabir et al

#### Open surgery

Huri, Acar, Binbay, Sozen <sup>45</sup> introduced a uro-oncology training course for 25 participants featuring open prostatic, scrotal and nephrectomy procedures on cadavers and on a 5-point satisfaction scale, the course was rated more than 3.2/5 for all elements, theoretical and practical. The surgical anatomy sections of the course were the most highly rated.

Cabello, Gonzalez, Quicios, Bueno, Garcia, Arribas, Clasca <sup>47</sup> describe a training model for open renal transplantation using Thiel embalmed cadavers in 28 participants. On a 10-point scale, the participants rated it 8.6/10 for utility and 8.9/10 for usefulness for daily clinical practice. However, the authors noted the lack of bleeding and the difficulties in determining the quality of vascular anastomosis.

Ahmed, Aydin, Dasgupta, Khan, McCabe <sup>54</sup> developed a cadaveric simulation course with the British Association of Urological Surgeons for 81 residents and 27 faculty including core open surgery, endourology and advanced trauma and emergency urological surgery. The procedures taught and simulated included both renal, prostate and bladder surgery as well as scrotal procedures such as testicular fixation and radical orchidectomy. The course demonstrated face validity with a mean of 3/5 on a 5-point Likert scale and >3/5 for content validity.

#### **Discussion**

# Summary of evidence

This is the first paper to systematically review and compare the use of cadaveric tissue, animal tissue and live animals in a wet lab simulation environment for urological surgery. Against a backdrop of restricted training time for surgical trainees in the present environment, the need for a representative, cost-effective and realistic wet lab model is imperative<sup>60</sup>, and this is clearly a growing issue with the earliest study being published in 2004. It is clear from reviewing the literature that wet lab simulation is being utilised across a range of procedures, however a clear bias towards the use of wet lab simulation for laparoscopic and endoscopic procedures. The reasons for this have not been formally elucidated, but it appears that the high level of dexterity required for successful procedures have driven innovation in training techniques, namely wet lab simulation.

It is lamentable that most studies are of poor quality with only a single study demonstrating 1b LoE being an RCT of good quality (albeit of small size with 29 participants) and 3 studies being randomised (but not necessarily controlled) studies with an average of 22.7 participants per study and demonstrated 2a LoE. No study demonstrated Level 1 LoR.

Overall, many studies were small, with a mode of 20 participants per study. This however this correlates with the findings of Van Nortwick, Lendvay, Jensen, Wright, Horvath, Kim <sup>14</sup>, who reviewed validity studies and found an average of 37 participants per study (Median=29). A significant proportion were often descriptive-only, demonstrating no more than Level 4 LoR. This is disappointing as many of the studies show promising potential but have not undergone comparative research.

The vast majority of studies featured face validation (72.1%) however vanishingly few studies demonstrated higher level validation with only 2 studies demonstrating concurrent validity and 2 studies on predictive validity. This is also consistent with the findings of Van Nortwick, Lendvay, Jensen, Wright, Horvath, Kim <sup>14</sup> who found only 24% of studies they reviewed demonstrated concurrent validity and 5% on predictive validity.

Most studies were in animal models which is to be expected from the discussions of authors highlighting the superior visual and tactile realism of animal models compared to bench-top dry lab models. However, within wet lab models, the realistic anatomy and tissue feel of cadavers means that it retains its 'gold standard' status in simulated training. The higher cost, poorer availability and ethical concerns related to use of this tissue, mean that it cannot be the sole method of wet lab simulation for surgical trainees. The numerous studies concerning animal models indicates the pertinence of this point.

The major point discussed in relation to cadaveric models is that animal models are cheaper and without the same ethical considerations (especially if using ex-vivo tissue models). Cadaver acquisition is beset with problems regarding culture, religion and the necessity for organ donation, which has therefore reduced the supply of appropriate tissue <sup>61</sup>, in conjunction with the increase in medical students, and subsequently, surgical trainees.

We have previously espoused a training algorithm for use in urology, suggesting trainees commence with virtual reality models and continue onto dry-lab models, followed by animal tissue and live animal models <sup>54</sup>. Cadaveric samples form a later stage of training, enabling the 'fine-tuning' of skills on the relatively scarce numbers of available cadavers. The general concordance of wet lab model usage between surgical specialties would suggest that this algorithm could be translated for use across numerous specialities with positive effects on patient safety and learning quality.

Virtual reality (VR) models have gained traction over recent years within certain specialities, including urology. A further extension to our work could systematically review the introduction of VR models into the variety of surgical fields.

We recommend the implementation of wet lab training methods from the earliest stages of surgical training to maximise learning within the limited time frame of formal teaching. As ex-vivo animal models are relatively affordable and have some educational value, they should be introduced early on within surgical training, progressing to in-vivo models and finally to cadaveric tissue.

#### Limitations

The studies exhibited significant heterogeneity and could not be used to perform a quantitative pooled meta-analysis. Additionally, many studies were excluded for being based on conference abstracts with insufficient information in addition to other grey literature potentially being excluded contributing to bias.

#### **Conclusions**

Simulation in surgical education is becoming more prevalent in the literature, with the value of wet lab simulation in early stages of training clearly demonstrated and cadaveric

simulation for more advanced procedures. There is currently a focus on animal rather than cadaveric simulation, possibly due to cost and ethical considerations. However, new techniques in embalming such as the Thiel method is improving the utility of cadaveric simulation. Studies are also predominately of a low level of evidence with higher level evidence, especially randomised controlled studies, needed to determine the most efficacious method of simulation.



#### References

- 1. McDougall EM. Validation of surgical simulators. *J Endourol* 2007;21:244-7.
- 2. Coxon JP, Pattison SH, Parks JW, et al. Reducing human error in urology: Lessons from aviation. *BJU Int* 2003;91:1-3.
- 3. McGreevy JM. The aviation paradigm and surgical education. *J Am Coll Surg* 2005;201:110-7.
- 4. Torkington J, Smith SG, Rees BI, et al. Skill transfer from virtual reality to a real laparoscopic task. *Surg Endosc* 2001;15:1076-9.
- 5. Andreatta PB, Woodrum DT, Birkmeyer JD, et al. Laparoscopic skills are improved with lapmentor<sup>TM</sup> training: Results of a randomized, double-blinded study. *Ann Surg* 2006;243:854-60.
- 6. Sedlack RE, Kolars JC. Computer simulator training enhances the competency of gastroenterology fellows at colonoscopy: Results of a pilot study. *The American Journal of Gastroenterology* 2004;99:33-7.
- 7. Wignall GR, Denstedt JD, Preminger GM, et al. Surgical simulation: A urological perspective. *J Urol* 2008;179:1690-9.
- 8. Aydin A, Raison N, Khan MS, et al. Simulation-based training and assessment in urological surgery. *Nat Rev Urol* 2016;13:503-19.
- 9. Aydin A, Shafi AM, Shamim Khan M, et al. Current status of simulation and training models in urological surgery: A systematic review. *J Urol* 2016;196:312-20
- 10. Brunckhorst O, Aydin A, Abboudi H, et al. Simulation-based ureteroscopy training: A systematic review. *J Surg Educ* 2015;72:135-43.
- 11. Morgan M, Aydin A, Salih A, et al. Current status of simulation-based training tools in orthopedic surgery: A systematic review. *J Surg Educ* 2017;74:698-716.
- 12. Musbahi O, Aydin A, Al Omran Y, et al. Current status of simulation in otolaryngology: A systematic review. *J Surg Educ* 2017;74:203-15.
- 13. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: The prisma statement. *PLoS Med* 2009;6:e1000097.
- 14. Van Nortwick SS, Lendvay TS, Jensen AR, et al. Methodologies for establishing validity in surgical simulation studies. *Surgery* 2010;147:622-30.
- 15. Tay C, Khajuria A, Gupte C. Simulation training: A systematic review of simulation in arthroscopy and proposal of a new competency-based training framework. *Int J Surg* 2014;12:626-33.
- 16. Carter FJ, Schijven MP, Aggarwal R, et al. Consensus guidelines for validation of virtual reality surgical simulators. *Surg Endosc* 2005;19:1523-32.
- 17. Jiang C, Liu M, Chen J, et al. Construct validity of the chicken crop model in the simulation of laparoscopic pyeloplasty. *J Endourol* 2013;27:1032-6.
- 18. Yang RM, Bellman GC. Laparoscopic urethrovesical anastomosis: A model to assess surgical competency. *J Endourol* 2006;20:679-82.
- 19. Laguna MP, Arce-Alcazar A, Mochtar CA, et al. Construct validity of the chicken model in the simulation of laparoscopic radical prostatectomy suture. *J Endourol* 2006;20:69-73.
- 20. Hung AJ, Ng CK, Patil MB, et al. Validation of a novel robotic-assisted partial nephrectomy surgical training model. *BJU Int* 2012;110:870-4.

- 21. Hung AJ, Patil MB, Zehnder P, et al. Concurrent and predictive validation of a novel robotic surgery simulator: A prospective, randomized study. *J Urol* 2012;187:630-7.
- 22. Soria F, Morcillo E, Serrano A, et al. Development and validation of a novel skills training model for retrograde intrarenal surgery. *J Endourol* 2015;29:1276-81.
- 23. Hu D, Liu T, Wang X. Flexible ureteroscopy training for surgeons using isolated porcine kidneys in vitro. *BMC Urol* 2015;15:23.
- 24. Teber D, Guven S, Yaycioglu O, et al. Single-knot running suture anastomosis (one-knot pyeloplasty) for laparoscopic dismembered pyeloplasty: Training model on a porcine bladder and clinical results. *Int Urol Nephrol* 2010;42:609-14.
- 25. Jutzi S, Imkamp F, Kuczyk MA, et al. 656 improved porcine ex-vivo organ model for percutaneous renal surgery (sandwich-model) using a laparoscopy-training-box (situs box). *European Urology Supplements* 2013;12:e656.
- 26. Cruz JA, Passerotti CC, Frati RM, et al. Surgical performance during laparoscopic radical nephrectomy is improved with training in a porcine model. *J Endourol* 2012;26:278-82.
- 27. Boon JR, Salas N, Avila D, et al. Construct validity of the pig intestine model in the simulation of laparoscopic urethrovesical anastomosis: Tools for objective evaluation. *J Endourol* 2008;22:2713-6.
- 28. Sabbagh R, Chatterjee S, Chawla A, et al. Transfer of laparoscopic radical prostatectomy skills from bench model to animal model: A prospective, single-blind, randomized, controlled study. *J Urol* 2012;187:1861-6.
- 29. Jutzi S, Imkamp F, Kuczyk MA, et al. New ex vivo organ model for percutaneous renal surgery using a laparoendoscopic training box: The sandwich model. *World J Urol* 2014;32:783-9.
- 30. Earp PP. Percutaneous renal surgery: New model for learning and training. *Int Braz J Urol* 2003;29:151-4.
- 31. Hacker A, Wendt-Nordahl G, Honeck P, et al. A biological model to teach percutaneous nephrolithotomy technique with ultrasound- and fluoroscopy-guided access. *J Endourol* 2007;21:545-50.
- 32. Hammond L, Ketchum J, Schwartz BF. A new approach to urology training: A laboratory model for percutaneous nephrolithotomy. *J Urol* 2004;172:1950-2.
- 33. Strohmaier WL, Giese A. Improved ex vivo training model for percutaneous renal surgery. *Urol Res* 2009;37:107-10.
- 34. Strohmaier WL, Giese A. Ex vivo training model for percutaneous renal surgery. *Urol Res* 2005;33:191-3.
- 35. Zhang Y, Ou TW, Jia JG, et al. Novel biologic model for percutaneous renal surgery learning and training in the laboratory. *Urology* 2008;72:513-6.
- 36. Mishra S, Kurien A, Ganpule A, et al. Surgical skills lab for percutaneous renal access training: Content validation comparison between live porcine and simulation model. *J Endourol* 2009;23:A212.
- 37. Jagtap J. Surgical skills lab for percutaneous renal access training: Content validation comparison between live porcine and vr simulation model. *J Urol* 2010;183:e515.
- 38. Grimsby GM, Andrews PE, Castle EP, et al. Urologic surgical simulation: An endoscopic bladder model. *Simul Healthc* 2011;6:352-5.
- 39. Khanna A, Horgan S. A laboratory training and evaluation technique for robot assisted ex vivo kidney transplantation. *Int J Med Robot* 2011;7:118-22.

- 40. Alemozaffar M, Narayanan R, Percy AA, et al. Validation of a novel, tissue-based simulator for robot-assisted radical prostatectomy. *J Endourol* 2014;28:995-1000.
- 41. Tiong HY, Goh B, Tan L, et al. Robotic assisted kidney auto-transplantation in a porcine skill training model. *European Urology Supplements* 2017;16:e2053.
- 42. Soria F, Morcillo E, Sanz JL, et al. Description and validation of realistic and structured endourology training model. *Am J Clin Exp Urol* 2014;2:258-65.
- 43. Marchini GS, Fioravanti ID, Jr., Horta LV, et al. Specific training for less surgery results from a prospective study in the animal model. *Int Braz J Urol* 2016;42:90-5.
- 44. Molinas CR. The rabbit nephrectomy model for training in laparoscopic surgery. *Hum Reprod* 2004;19:185-90.
- 45. Huri E, Acar C, Binbay M, et al. Cadaveric urooncologic anatomic dissection course: A novel training method in surgical practice. *J Endourol* 2010;24:A63.
- 46. Page T. The use of fresh frozen cadavers for the teaching of holmium laser enucleation of prostate, thulium prostate resection and high power ktp laser vapourisation. *BJU Int* 2015;115:16-76.
- 47. Cabello R, Gonzalez C, Quicios C, et al. An experimental model for training in renal transplantation surgery with human cadavers preserved using w. Thiel's embalming technique. *J Surg Educ* 2015;72:192-7.
- 48. Huri E, Skolarikos A, Tatar I, et al. Simulation of rirs in soft cadavers: A novel training model by the cadaveric research on endourology training (cret) study group. *World J Urol* 2016;34:741-6.
- 49. Blaschko SD, Brooks HM, Dhuy SM, et al. Coordinated multiple cadaver use for minimally invasive surgical training. *Journal of the Society of Laparoendoscopic Surgeons* 2007;11:403-7.
- 50. Raison N, Ahmed K, Aydin A, et al. Novel cadaveric robotic training programme. *J Endourol* 2015;29:A74.
- 51. Mains E, Tang B, Golabek T, et al. Ureterorenoscopy training on cadavers embalmed by thiel's method: Simulation or a further step towards reality? Initial report. *Cent European J Urol* 2017;70:81-7.
- 52. Rai BP, Tang B, Healy S, et al. Face validity study of cadavers using thiel method of embalming for endoscopic surgery in urology. *Urology* 2014;84:S137.
- 53. Ozcan S, Huri E, Tatar I, et al. Impact of cadaveric surgical anatomy training on urology residents knowledge: A preliminary study. *Turk J Urol* 2015;41:83-7.
- 54. Ahmed K, Aydin A, Dasgupta P, et al. A novel cadaveric simulation program in urology. *J Surg Educ* 2015;72:556-65.
- 55. Bowling CB, Greer WJ, Bryant SA, et al. Testing and validation of a low-cost cystoscopy teaching model: A randomized controlled trial. *Obstet Gynecol* 2010;116:85-91.
- 56. De Win G, Van Bruwaene S, Allen C, et al. Design and implementation of a proficiency-based, structured endoscopy course for medical students applying for a surgical specialty. *Adv Med Educ Pract* 2013;4:103-15.
- 57. Chou DS, Abdelshehid C, Clayman RV, et al. Comparison of results of virtual-reality simulator and training model for basic ureteroscopy training. *J Endourol* 2006;20:266-71.
- 58. Ogan K, Jacomides L, Shulman MJ, et al. Virtual ureteroscopy predicts ureteroscopic proficiency of medical students on a cadaver. *J Urol* 2004;172:667-71.

59. Ramachandran A, Kurien A, Patil P, et al. A novel training model for laparoscopic pyeloplasty using chicken crop. *J Endourol* 2008;22:725-8.

- 60. Khan R, Aydin A, Khan MS, et al. Simulation-based training for prostate surgery. *BJU Int* 2015;116:665-74.
- 61. Krahenbuhl SM, Cvancara P, Stieglitz T, et al. Return of the cadaver: Key role of anatomic dissection for plastic surgery resident training. *Medicine (Baltimore)* 2017;96:e7528.



# **Figures and Tables**

Fig. 1. PRISMA Flow diagram as per Moher et al<sup>13</sup>

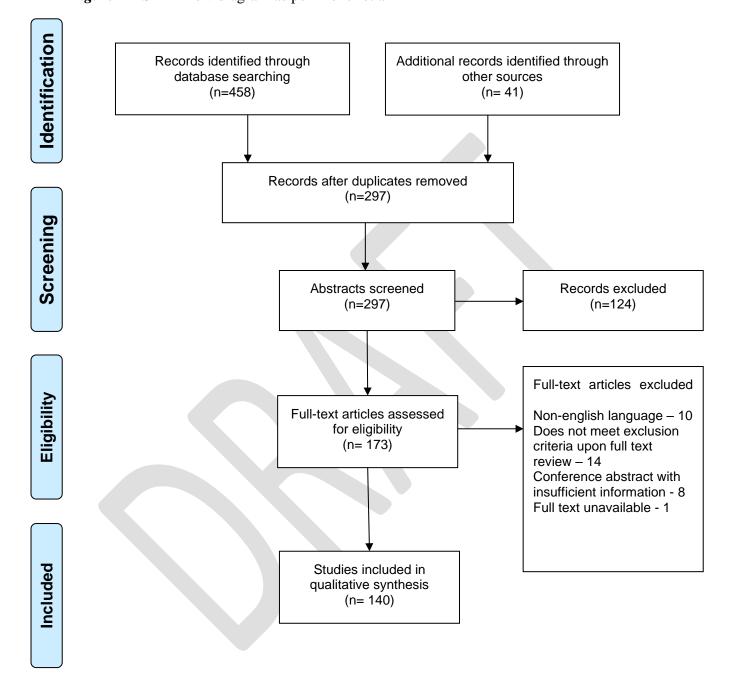


Table 1. Advantages and disadvantages of wet lab simulation methods							
Simulation method	Advantages	Disadvantages					
Animal tissues	Cost-effective, real tissue	Single-use, difficulties in storage					
Live animals	Good face validity, can do full	Single-use, Ethical issues, cost,					
	procedure	special procedures, anatomical					
		differences					
Cadavers (Fig. 1)	Best face validity, haptic	Single-use, cost, availability,					
Prisma flow diagram as per	feedback, full procedure,	infection risk					
Moher, Liberati, Tetzlaff,	realistic tissue, 'the gold						
Altman, PRIMSA group <sup>13</sup>	standard'						

Table 2. Characteristics of included studies (n=140)					
Study profile	n (%)				
Type of simulation					
Animal	31 (72.1)				
Ex-vivo	21				
In-vivo	9				
Cadaveric	12 (27.9)				
Animal model used					
Pig	26				
Chicken	4				
Rabbit	1				
Validity focus					
Face	31				
Content	18				
Construct	17				
Concurrent	2				
Predictive	2				
Transfer	3				
Levels of evidence					
1b	1				
2a	3				
2b	26				
3	13				
Levels of recommendation					
2	4				
3	24				
4	13				

**Supplementary Table 1. Search strategy** 

# CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

		T
1	exp Surgical Procedures, Operative/	(7220088)
2	exp Specialties, Surgical/	(4422497)
3	exp surgery/	(4265000)
	(surg\$ or microsurg\$).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx,	
4	ui, sy]	(5734468)
5	or/1-4	(9210386)
6	ed.fs.	(262111)
	education, graduate/ or education, medical, graduate/ or education, medical/ or	
7	education, medical, continuing/	(338400)
8	medical education/	(260274)
	educat\$ or train\$ or learn\$ or teach\$).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx,	
9	nm, kf, px, rx, ui, sy]	(3561617)
10	or/6-9	(3633187)
11	5 and 10	(422781)
12	Surgical training/	(17128)
13	11 or 12	(422781)
14	wet lab\$.mp.	(1777)
	in-vivo or ex-vivo or fresh frozen or porcine or animal model\$).mp. [mp=ti, ab, hw,	(= / / /
15	tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, ui, sy]	(3181469)
16	Cadaver/	(84352)
17	cadaver\$.mp.	(155311)
	(porcine or pig\$1).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, ui,	(100011)
18	sy]	(666576)
19	or/14-18	(3751832)
20	13 and 19	(17427)
21	exp *Surgical Procedures, Operative/ or exp *Specialties, Surgical/ or exp *surgery/	(4099004)
22	(surg\$ or microsurg\$).tw.	(3963558)
23	or/21-22	(6537482)
24	20 and 23	(13476)
24		(13470)
25	exp *Surgical Procedures, Operative/ed or exp *Specialties, Surgical/ed or exp	(25046)
25	*surgery/ed	(23040)
26	*education, graduate/ or *education, medical, graduate/ or *education, medical/ or	(105764)
26	*education, medical, continuing/ or *medical education/	(185764)
27	*Surgical training/	(8131)
28	educat\$ or train\$ or learn\$ or teach\$).tw.	(2708345)
29	or/25-28	(2777956)
30	24 and 29	(12524)
31	*Cadaver/	(7623)
	(wet lab\$ or (in-vivo or ex-vivo or fresh frozen or porcine or animal model\$) or	(2005-
32	cadaver\$ or (porcine or pig\$1)).tw.	(2827026)

# CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

33	or/31-32	(2830433)
34	30 and 33	(10216)
35	(educat\$ or train\$ or learn\$ or teach\$).ti.	(848296)
36	27 or 35	(851281)
37	34 and 36	(3662)
38	(surg\$ or microsurg\$).ti.	(1275498)
39	transplant\$.ti.	(551385)
40	operative.ti.	(77743)
41	or/38-40	(1882968)
42	37 and 41	(1555)
43	35 and 42	(1474)
	(wet lab\$ or (in-vivo or ex-vivo or fresh frozen or porcine or animal model\$) or	
44	cadaver\$ or (porcine or pig\$1)).ti.	(747603)
45	43 and 44	(439)
46	remove duplicates from 45	(254)

Supplementary Ta	Supplementary Table 2. Types of validity as per McDougall <sup>1</sup> , Van Nortwick,					
Lendvay, Jensen,	Wright, Horvath, Kim <sup>14</sup> and Tay, Khajuria, Gupte <sup>15</sup>					
Type of validity	Definition					
Face	Opinions, including of nonexperts, regarding the realism of the					
	simulator – does the simulator represent what it is supposed to					
	represent					
Content	Opinions of experts about the simulator and its appropriateness for					
	training – does the simulator teach what it is supposed to teach					
Construct A	Within one group — Ability of the simulator to assess and					
	differentiate between the level of experience of an individual or group					
	measured over time					
Construct B	Between groups — Ability of the simulator to distinguish between					
	different levels of experience					
Concurrent	Comparison of the new model against the older and gold standard,					
	usually by Objective Structured Assessment of Technical Skills					
	(OSATSs)					
Transfer	A measure of whether the simulator has the effect that it proposes to					
	have – does the simulator produce a learning effect and improve					
	performance with continued use					
Predictive	Correlation of performance with operating room performance, usually					
	measured by OSATS					

# CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

Supple	Supplementary Table 2A. Levels of evidence						
Level	Criteria						
1a	Systematic reviews (meta-analysis) containing at least some trials of level 1b evidence, in which results of separate, independently conducted trials are consistent						
1b	Randomised controlled trial of good quality and of adequate sample size (power calculation)						
2a	Randomised trials of reasonable quality and/or of inadequate sample size						
2b	Non-randomised trials, comparative research (parallel cohort)						

Non-randomised, non-comparative trials, descriptive research

Expert opinions, including the opinion of Work Group members

Non-randomised trials, comparative research (historical cohort, literature controls)

2c

3

4

Supple	Supplementary Table 2B. Levels of recommendation						
Level	Criteria						
1	Based on one systematic review (1a) or at least two independently conducted research projects classified as 1b						
2	Based on at least independently conducted research projects classified as level 2a or 2b, within concordance						
3	Based on one independently conducted research project level 2b, or at least two trials of level 3, within concordance						
4	Based on one trial at level 3 or multiple expert opinions, including the opinion of Work Group members (e.g., level 4)						

CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

Supplementary Table 3. Laparoscopic urological surgery models										
Reference	Type of simulation			Procedure	Subjects	Validation type	LoE	LoR		
Molinas 2004 <sup>44</sup>	Animal	Rabbit	In-vivo	Laparoscopic nephrectomy	20	Face; content; construct	2b	3		
Cruz 2012 <sup>26</sup>	Animal	Porcine	In-vivo	Laparoscopic radical nephrectomy	6	Face; content; transfer	2b	3		
De Win 2013 <sup>56</sup>	Animal	Porcine	Ex-vivo	Laparoscopic radical nephrectomy	22	Content, construct	2b	3		
Marchini 2016 <sup>43</sup>	Animal	Porcine	In-vivo	Total nephrectomy (SILS)	15	Face; content	2b	3		
Ramachandran 2008 <sup>59</sup>	Animal	Chicken	Ex-vivo	Laparoscopic pyeloplasty	3	Construct	3	4		
Jiang 2013 <sup>17</sup>	Animal	Chicken	Ex-vivo	Laparoscopic pyeloplasty	15	Construct	2b	3		
Teber 2010 <sup>24</sup>	Animal	Porcine	Ex-vivo	Laparoscopic pyeloplasty	5	Construct	2b	3		
Yang 2006 <sup>18</sup>	Animal	Chicken	Ex-vivo	Laparoscopic Urethrovesical Anastomosis	8	Content; construct	2b	3		
Laguna 2006 <sup>19</sup>	Animal	Chicken	In-vivo	Laparoscopic Urethrovesical Anastomosis	5	construct	2b	3		
Boon 2008 <sup>27</sup>	Animal	Porcine	Ex-vivo	Laparoscopic urethrovesical anastomosis	12	Face; content; construct	2b	3		
Sabbagh 2012 <sup>28</sup>	Animal	Porcine	In-vivo	Laparoscopic urethrovesical anastomosis	28	Face	2a	2		

LoE: level of evidence; LoR: level of recommendation.

CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

Supplementary Table 4. Endourology models										
Reference	Type of simulation			Procedure	Subjects	Validation type	LoE	LoR		
Grimsby 2011 <sup>38</sup>	Animal	Porcine	Ex-vivo	Rigid cystoscopy; bladder biopsy	2	Construct; transfer	2b	3		
Soria 2014 <sup>42</sup>	Animal	Porcine	Ex-vivo	Urethrocystoscopy	40	Face; content; construct	2b	3		
Bowling 2010 <sup>55</sup>	Cadaver			Urethrocystoscopy	29	Construct	1b	2		
Hu 2015 <sup>23</sup>	Animal	Porcine	In-vivo	Flexible ureteroscopy	20	Face; construct	2b	3		
Chou 2006 <sup>57</sup>	Animal	Porcine		Ureterorenoscopy	16	Concurrent	2a			
Ogan 2004 <sup>58</sup>	Cadaveric			Diagnostic ureteroscopy	32	Construct, predictive	2b			
Mains 2017 <sup>51</sup>	Cadaveric			Semi-rigid and flexible ureterorenoscopy	8	Face; content	3	4		
Rai 2004 <sup>52</sup>	Cadaveric			Ureterorenoscopy; transurethral resection of prostate	11	Face	2b	3		
Soria 2015 <sup>22</sup>	Animal	Porcine	In-vivo	Endoscopic retrograde intrarenal surgery	60	Face; content; construct	2b	3		
Huri 2016 <sup>48</sup>	Cadaveric			Retrograde intrarenal surgery	12	Face; content; construct	2b	3		
Mishra 2010 <sup>36</sup>	Animal	Porcine	Ex-vivo	Percutaneous renal puncture	24	construct	2b	3		
Earp 2003 <sup>30</sup>	Animal	Porcine	Ex-vivo	Percutaenous lithotripsy and endopielotomy		Face	3	4		

CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

Hammond 2008 <sup>32</sup>	Animal	Porcine	Ex-vivo	Percutaneous nephrolithotomy		Face	3	4
Zhang 2008 <sup>35</sup>	Animal	Porcine	Ex-vivo	Percutaneous renal manipulations	42	Face	2b	3
Hacker 2007 <sup>31</sup>	Animal	Porcine	Ex-vivo	Percutaneous nephrolithotomy		Face	3	4
Strohmaier 2009 <sup>33</sup>	Animal	Porcine	Ex-vivo	Percutaneous nephrolithotomy		Face	3	4
Strohmaier 2005 <sup>34</sup>	Animal	Porcine	Ex-vivo	Percutaneous nephrolithotomy		Face	3	4
Jagtap 2010 <sup>37</sup>	Animal	Porcine	In-vivo	Percutaneous renal puncture	24	Face; content	2b	3
Jutzi 2013 <sup>25</sup>				Minimally invasive percutaneous				
Jui21 2013	Animal	Porcine	Ex-vivo	nephrolithotomy	7	Face	3	4
Jutzi 2014 <sup>29</sup>				Minimally invasive percutaneous				
Jul 2014	Animal	Porcine	Ex-vivo	nephrolithotomy	11	Face	3	4
				Holmium laser enucleation of prostate;				
Page 2015 <sup>46</sup>				Thulium prostate resection; high power				
	Cadaveric			KTP laser vaporization		Face; content	3	4

LoE: level of evidence; LoR: level of recommendation.

CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

Supplementary Table 5. Robotic urological surgery models										
Reference	Type of simulation			Procedure	Subjects	Validation type	LoE	LoR		
Hung 2012 <sup>20</sup>	Animal	Porcine	Ex-vivo	Robot-assisted partial nephrectomy	46	Face; content; construct	2b	3		
Hung 2012 <sup>21</sup>	Animal	Porcine	Ex-vivo	Robotic bowel resection; robotic cystotomy and repair; robotic partial nephrectomy	24	Concurrent; predictive	2a	2		
Khanna 2011 <sup>39</sup>	Animal	Porcine	Ex-vivo	Robot-assisted ex-vivo kidney transplantation		Face	2b	3		
Tiong 2017 <sup>41</sup>	Animal	Porcine	In-vivo	Robot-assisted kidney transplantation		Face; content	3	4		
Alemozaffar 2014 <sup>40</sup>	Animal	Porcine	Ex-vivo	Robot-assisted radical prostatectomy	20	Face; content; construct	2b	2		
Blaschko 2007 <sup>49</sup>	Cadaveric			Robot-assisted laparoscopic prostatectomy; cardiac surgery	22	Face	3	4		

CUAJ – Review Al-Jabir et al Review: Status of wet lab and cadaveric simulation in urological training

Raison 2014 <sup>50</sup>	Cadaveric	Robotic radical cystectomy; robotic radical prostatectomy; robotic extended lymph node dissection; robotic radical		Face; content;		
		Tymph hode dissection, foodic fadical		race, content,		
		nephrectomy	16	construct	2b	3

LoE: level of evidence; LoR: level of recommendation.

Supplementary Table 6. Open urological surgery models								
Reference	Type of simulation			Procedure	Subjects	Validation type	LoE	LoR
Ozcan 2015 <sup>53</sup>	Cadaveric			Urological anatomy dissection	50	Face; transfer	3	4
Huri 2010 <sup>45</sup>				Radical prostatectomy; inguinal				
				orchiectomy; retroperitoneal lymph node				
				and pelvic lymph node dissection;				
				nephrectomy; adrenalectomy; radical				
				cystectomy; extended lymph node				
	Cadaveric			dissection	25	Face; content	2b	3
Cabello 2014 <sup>47</sup>	Cadaveric			Renal transplantation	28	Face	2b	3
Ahmed 2015 <sup>54</sup>	Cadaveric			Various urological procedures	102	Face; content	2b	3

LoE: level of evidence; LoR: level of recommendation.