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Human cadavers as an experimental model for esophageal surgery

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SUMMARY. **The use of cadavers in experimental esophageal surgery is reviewed. Items useful to cadaveric studies such as post-mortem changes, biosafety, ethics, and legislation are discussed. Tactics used in minimally invasive procedures (thoracoscopy and laparoscopy) are shown. Cadaveric use in studies concerning esophagectomy, gastroesophageal reflux disease, esophageal atresia, Boerhaave's syndrome, and Mallory–Weiss tears are discussed. It is concluded that human bodies represent a good but underused model for esophageal surgery.**

INTRODUCTION

The history of medicine is full of anecdotal and curious facts concerning the study of human cadavers. Dissection of human bodies has been prohibited[1] and stimulated in such a way that artists dissected corpses to be anatomically perfect in their paintings and sculptures.[1,2]

None can deny the progress in the fields of anatomy and physiology that cadaveric studies enabled. In the beginnings of surgery, human bodies made their contribution as well. At present, human corpses are extensively used in anatomic studies and for teaching purposes. However, as a model for experimental surgery, in our opinion, they are underused.

We review the basic concepts linked to cadaver usage and cadaveric experiments in esophageal surgery.

POST-MORTEM CHANGES

With extinction of life, cadaveric phenomena start, some of which are of interest to the research surgeon.

Visceral topography and relationship

After death, the diaphragm relaxes, lifting the abdominal viscera, which is the same condition seen during anesthesia.[3]

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Rigor mortis

Death brings a phenomenon of muscular rigidity, rigor mortis.[4–6] Rigor develops in both smooth and striped skeletal muscles.[6]

Rigor's time of appearance and disappearance may be modified by various factors.[4–6] Generally, it starts in the smooth muscles and diaphragm as soon as 2 h after death. Skeletal muscles (thoracic and abdominal wall muscles are of interest) start to stiffen after 3–6 h. Rigidity is progressively increased until it reaches maximal strength at 24 h and then disappears after 36–48 h.

Once established, rigor can be broken by stretching the involved muscle.[6]

Dehydration

Dehydration is not significant in adult cadavers.[5] Weight is preserved for a long period of time. Exposed mucosae become dehydrated quickly, while non-exposed mucosae are not significantly affected.

Putrefaction

Cadavers in which putrefaction is manifested, for obvious reasons, are not good candidates for experimental surgery.

Numerous environmental factors, previous health status, body constitution, cause of death, and, naturally, conservative procedures can modify the onset of putrefaction.[4–6] Usually, it can be noticed 24–36 h after death.[4–6] The first manifestation is the greenish discoloration of the abdominal lower right quadrant.[4–6]

Conservative procedures

Frequently, fresh corpses are used in surgical protocols; however, for the purpose of preventing or retarding putrefaction, some conservative procedures can be utilized in the cadaver to be used in experimental surgery. Techniques most used are refrigeration and embalming (preserving fluids injected in arteries and cavities).

Changes produced by conservative procedures have only forensic interest, and they are not significant for experimental surgery.[6,7]

BIOSAFETY

Although there is no evidence of a higher risk of human immunodeficiency virus (HIV) transmission in autopsy personnel,[8–10] it must be considered that handling human cadavers carries the same likelihood of contamination as operating on live patients or manipulating any biologic material. Full precautions and protection equipment must be used.[10–12]

Hepatitis is also a concern. Pathologists and embalmers were found to be at increased risk of infection with the hepatitis B virus.[10,13]

Other transmittable diseases are also risks, but they are preventable using the correct precautions.[10,14]

Embalming with formaldehyde-based chemicals produces a satisfactory reduction in microbial flora,[15] although pathogenic organisms have been recovered from embalmed human remains.[16–18]

ETHICS AND LEGISLATION

> 'It is impossible for the surgeon to become expert in all of the intricate legal issues associated with human experimentation, but it is his responsibility to be fully aware of the guidelines, codes, and modern discussions which have clearly outlined many of the moral problems.'[19]

Ethics

There are more discussions and controversies than legislation and consensus surrounding the use of cadavers for scientific purposes.

It has not been established which kind of cadavers should be used in experiments.

Historically, ethics was linked to and governed by religion. Human corpse dissection was prohibited by the Church[1] and then was allowed again. Bodies unclaimed, such as criminals and those from asylums, have been utilized in dissections and experiments. Science also defied religion and the law, dissecting cadavers stolen from their graves or even murdered for that purpose.[1,2,20,21]

Today, religion is no longer an obstacle, apart from individual misinterpretation. The three most important occidental religions, Christianity, Judaism and Islam, are not opposed to autopsy, and they consider use of the dead to help the living an act of altruism and goodness.[20,22] Ethical discussions, nonetheless, persist.

Issues such as the practice and teaching of invasive and non-invasive procedures in the newly dead are still being debated.[23–40]

Although the use of dead bodies in experimental surgery can occur in the situation of life donation specifically for this purpose or using unclaimed bodies 'donated' to anatomic laboratories, frequently the most common situation is the use of fresh cadavers submitted for clinical autopsies. This situation is rarely discussed ethically and legally. Each university has its own policy.[41]

In our health service, when relatives are asked to agree to a clinical autopsy they are informed that the body can be used for teaching and scientific purposes. In case of specific protocols, written permission is also obtained. Life donation is not habitual in Brazil.

Legislation

In most countries (if not all), laws govern only organ and tissue transplantation, and cadaver donation for the anatomy laboratories of medical schools.[1,4,21,42–49] Usually, scientific experimentation is more an issue for ethics committees than legislators.

MINIMALLY INVASIVE SURGERY

Thoracoscopy

Thoracoscopy is valuable in post-mortem examinations.[50,51] Although cadaveric thoracoscopy has been most enthusiastically used by neurosurgeons interested in access to the spine,[52–55] esophageal dissection has also been performed.[56]

The main, and probably unique, problem found in post-mortem thoracoscopy is the lungs, which are kept inflated after death. Caputy *et al.*[53] removed the lungs through a contralateral thoracotomy: an easy way to be rid of them, but, in our opinion, a condition that does not mimic life status. Cadaver rotation has been cited as a maneuver for moving the lungs.[50] Other groups do not report problems with the lungs or simply keep them apart with the aid of retractors.[52–55]

Laparoscopy

Laparoscopy in cadavers has been used by general surgeons[57–61] as well by other surgical specialties.[62–65]

It has also been used in autopsies.[66–69] Esophageal surgery has also been performed. Johnson *et al.*[70] tested laparoscopic Collis gastroplasty in the cadaver laboratory before the technique was started clinically.

Rigor mortis of the abdominal wall muscles is a dilemma during inflation of the cavity during pneumoperitoneum creation.[68,71,72] Arterial injection of ethanol and glycerin followed by vigorous massage has been described as a method for reducing rigor.[58] Clotteau and Premont[66,71,73] state that laparoscopy can be performed even in fresh, embalmed and refrigerated bodies by inflating the abdominal cavity with compressed air until the abdominal wall muscles are distended and rigor broken. Then pressure can be maintained using conventional laparoscopic insufflators. González Supery and Sainz[64] simply, but unnaturally, resected the abdominal wall.

Other authors[65,67,72] do not report problems with pneumoperitoneum creation.

One interesting method applied by González Supery and Sainz[64] is the injection of colored latex into the venous system to emphasize organ irrigation.

ESOPHAGEAL SURGERY

Esophagectomy

Although cadavers seem to be a natural model for esophagectomy, they have not been extensively used for this purpose. In the origins of esophageal resection, bodies helped in the search for the possible route to the esophageal bed at a time before mechanical ventilators. At present, they are almost forgotten.

Denck,[74] as a transhiatal esophagectomy pioneer, utilized human cadavers to test his new technique of 'stripping' and his new instrument, which was developed for this purpose.

Nassiloff[75] attempted an extra-pleural access to the esophagus in cadavers.

Vasconcelos[76] practiced in cadavers before performing the first esophagectomy in Brazil.

Our group is currently investigating the efficacy of mediastinal lymphadenectomy in transhiatal esophagectomy, and comparison of transhiatal esophagectomy with and without a diaphragm opening.

Gastroesophageal reflux disease

Gastroesophageal reflux disease is perhaps the surgical disease of the esophagus to which cadaveric experimental surgery made the best contribution. Reflux physiology was studied in the stomach and esophagus both isolated[77–82] and *in situ*.[83] New antireflux valves were tested[80,84] and old ones were evaluated.[83,85–88]

Experiments consisted of testing the natural antireflux mechanisms or those created by the fundoplication, independent of lower esophageal sphincter activity. Accordingly, the stomach was inflated with water until it refluxed into the esophagus, with or without a fundoplication, and the pressure of the reflux determined.[79,80,82–88] DeMeester *et al.*[78] and Gotley *et al.*[81] tried to simulated lower esophageal sphincter activity by applying external strain to the esophagus in a pressurized chamber.

Smooth muscle rigor must be remembered when working in experiments with esophageal and gastric pressures. Even if cadavers with the same postmortem interval are used, rigor can be variable. A simple method for equalizing the results is to partially inflate the organ to be used to break the rigor.

Esophageal atresia

Cadavers have been poorly used in experimental pediatric surgery, perhaps owing to the scarcity of children's corpses, and ethical and emotional issues involving infant cadaver usage.

Utilizing isolated esophagus from children's cadavers, Takada *et al.*[89] measured the effect of circular esophageal myotomies in elongating the esophagus and reducing anastomosis tension, in a simple experiment concerning experimental surgical treatment of esophageal atresia using a wide gap.

Boerhaave's syndrome

Boerhaave's syndrome is believed to have a barogenic basis. Cadavers have been used to help comprehend its pathophysiology since the nineteenth century.[90,91] Experiments consisted of over-distending the esophagus, which was proximally occluded until blasting, and either inflating the esophagus[90,92–95] or stomach[96,97] with air[92–97] or water,[90] *in situ*[92–96] or in isolated organs.[90,94,96,97] The rupture pressure and location of disruption were recorded. Derrick *et al.*,[93] interestingly, stripped away the lower esophageal mucosa through a gastrotomy, trying to link Boerhaave's syndrome to esophageal ulceration.

Although not mentioned by these authors, we believe that smooth muscle rigor must be remembered when working on experiments with esophageal and gastric pressures.

Houck and Griffin[98] also measured the pressure required to rupture the esophagus, but with the purpose of explaining the pathophysiology of spontaneous linear tears of the stomach in newborns.

Mallory–Weiss tears

Mallory and Weiss,[99] trying to explain esophageal perforation, occluded the pylorus, constricted the esophagus and compressed the partially filled stomach of cadavers. Before exploding the esophagus, they found the vertical linear tears that have been given their names.

CONCLUSION

Although the use of cadavers in research has some limitations (some physiological aspects and bleeding cannot be assessed in dead subjects), the advantages are abundant, particularly concerning the similarity of anatomy with patients rather than laboratory animals.

This paper shows that most esophageal surgery is feasible in cadavers.

We conclude that human cadavers provide a good but underused model for esophageal surgery.

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