

The Healing Scalpel

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Increased Utility of Sentinel Lymph Node Biopsy

Sentinel lymph node (SLN) biopsy is a technique that is based on the premise that the first draining lymph node of a tumor, known as the sentinel lymph node, is an accurate predictor of the presence of metastases in the draining nodal basin. Clinically positive axillary nodes are widely considered a contraindication to SLN biopsy in breast cancer, yet there is little data to support this claim. Although SLN biopsy has become the new pinnacle for axillary node staging in breast cancer and has utility in almost all patients with nonmetastatic disease, many authorities still consider palpable axillary nodes to be a contraindication. If the surgeon believes there to be palpable axillary nodes, is a SLN biopsy a valid option? To answer this question, investigators¹ at Memorial Sloan Kettering Cancer Center², one of the leading cancer institutes in the world, looked at the results of 106 patients of which the surgeon was either moderately suspicious (n=62) or highly suspicious (n=44) of axillary disease on the basis of palpation. SLN biopsy was performed in all patients, revealing that clinical examination of the axilla was inaccurate in 41% of the 106 patients. Clinical axillary examination yielded false-positive results in 33 of 62 patients (53%) diagnosed with moderately suspicious nodes and in 10 of 44 patients (23%) with highly suspicious nodes. In light of these results, Specht et al propose an increased utility of the SLN biopsy due to the relative inaccuracy of the clinical examination.

The manuscript by Specht et al.¹ emphasizes that SLN biopsy is more accurate than simple palpation of the axilla in determining the need for axillary dissection. However, these findings are based on patients examined by

2 selected surgeons and are not representative of all patients with a clinically positive axilla. Nevertheless, it seems that clinical examination alone yields a surprising incidence of false-positive results in patients in whom palpation suggests axillary involvement. The authors conclude that when pre-operative palpation or ultra sound guided fine needle aspirations are nondiagnostic, the SLN biopsy is a preferred and promising alternative to routine axillary lymph node dissection for breast cancer patients.

1. Specht MC, Fey JV, Borgen PI, Cody HS 3rd. Is the clinically positive axilla in breast cancer really a contraindication to sentinel lymph node biopsy? *J Am Coll Surg* 2005;200:10-14.
2. <http://www.mskcc.org/mskcc/html/44.cfm>

Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

Prostate cancer has the highest rate of incidence among American males, with 173.8 new cases diagnosed per 100,000 men, as reported by the Surveillance, Epidemiology and End Results (SEER) of National Cancer Institute.¹ However, the outlook for men diagnosed with the disease has improved, as over the past 20 years, overall survival rates for all stages of prostate cancer have dramatically increased. Current treatment options for prostate cancer include watchful waiting (the delay of treatment until signs of cancer progression are seen), surgery, chemotherapy, radiation, and/or hormonal therapy. Researchers at the Scandinavian Prostate Center published a recent article² in the *New England Journal of Medicine*,

which reported that radical prostatectomy reduces the risk of metastasis and disease progression among men diagnosed with early prostate cancer when compared to the watchful waiting approach.

In this recent clinical trial, Bill-Axen et al. studied men who presented with newly diagnosed, untreated prostate cancer to investigate the hypothesis that the relative reduction in the risk of death due to prostate cancer after surgery increases over time and that radical prostatectomy significantly improves overall survival. Between 1989 and 1999, researchers randomly assigned 695 males diagnosed with early prostate cancer to receive either a radical prostatectomy (347) or to engage in watchful waiting (348) as a means of treatment. After an average of eight years of follow up, 83 (23.9%) men who had been part of the group who received radical prostatectomy had died compared to 106 (30.5%) men from the watchful waiting group. Among the 347 men who had undergone surgery, 30 (8.6%) died from prostate cancer, compared to 50 (14.4%) of the 348 men who were assigned to watchful waiting. Researchers noted that the incidence of cumulative death from prostate cancer rose over time and increased from 2% after five years to 5.3% after 10 years. The same trend was also seen for distant metastasis and local disease progression.

The authors concluded that the radical prostatectomy is associated with a statistically significant reduction in main end points investigated in this study, with a relative reduction of 44% in mortality due to prostate cancer, 26% in overall mortality, 40% in the risk of distant metastasis, and 67% in local progression. The reduction in disease-specific mortality as a result of radical prostatectomy was greatest in patients younger than 65. Researchers admit that although this reduction in mortality is small, the reduced risk of metastasis and local disease progression are substantial. It is believed that the results from this study will help in guiding therapy and that the benefits of this surgery may be more obvious in longer periods of follow-up. Due to the fact that some men with early prostate cancer may be at a higher risk of cancer progression than others, patients are encouraged to speak with their physician regarding the individual risks and benefits of each treatment regimen.

1. http://seer.cancer.gov/csr/1975_2002/results_single/sect_01_table.04_2pgs.pdf
2. Bill-Axelsson A and Scandinavian Prostate Cancer Group Study No. 4. Radical prostatectomy versus watchful waiting in early prostate cancer. *N Engl J Med* 2005;352:1977-84.

Laparoscopic versus Open Cholecystectomy in Acute Cholecystitis

Laparoscopic cholecystectomy has almost come to replace the more conventional elective open procedure. However, the question remains of whether the surgeon should opt for an open procedure over a laparoscopic procedure for patients with acute cholecystitis. Using a double blind study

design, Johansson et al¹ randomized 70 patients with acute cholecystitis to receive a cholecystectomy with either an open or a laparoscopic approach. The mean age, gender, and duration of pre-operative symptoms were similar in both groups, as were the frequency of intraoperative cholangiography and the presence of common duct stones. Both postoperative sick leave and morbidity rates were similar between the two groups. The open procedure was associated with a shorter operating time and the laparoscopic approach with a shorter postoperative hospital stay. Both procedures had almost identical direct medical costs, as well as very similar indirect medical costs. Of interest, 8 laparoscopic procedures required conversion to an open procedure.

Conservative treatment of acute cholecystitis often leads to a delayed cholecystectomy. This delay of operation causes a longer hospital stay and yields a higher percentage of treatment failure. This study suggests that laparoscopic cholecystectomy can be performed successfully in patients with acute cholecystitis, thus avoiding a prolonged waiting period with the possibility of recurrent attacks or deterioration. However, the conversion rate is considerable, leading to increased costs and operating time, although the final outcome is not affected. Both techniques therefore offer low morbidity and rapid postoperative recovery.

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Herniorrhaphy - Azoospermia - Consent - Cryopreservation

Annually, about 600,000 patients in United States go through operations which involve the placement of a knitted polypropylene monofilament mesh prosthesis to patch the defect in the floor of the inguinal canal.^{1,2} This mesh, being a foreign body, ultimately leads to the formation of scar tissue that strengthens the area, thus preventing hernia recurrences. However, the vas deferens runs through this canal and the effects of the polypropylene mesh plug on this key fertility structure are unclear.

A study by Honig et al³ reports a multi-institutional experience of 14 men with azoospermia secondary to polypropylene mesh herniorrhaphy. The subjects were evaluated at eight institutions in the US, with a mean patient age of 35.5 years. On average, the men had a 1.8-year period of infertility, with the urologic evaluation occurring 6.3 years after herniorrhaphy. The hernia repair was open in ten patients, laparoscopic in two, and both in two. The vas obstruction was bilateral in nine patients and unilateral in five. Surgical exploration revealed a dense fibroblastic response encompassing the

polypropylene mesh with the vas deferens being either trapped or obliterated in all patients. Vasal reconstruction was performed in eight patients. Of the four patients with data available for analysis, two were able to impregnate their partners.

Findings from this study indicate that obstructive azoospermia can occur after herniorrhaphy with polypropylene mesh. Thus, the authors emphasize that: "before standard herniorrhaphy or herniorrhaphy using mesh, young men need to be advised of the potential risk of vasal obstruction and possible compromise of their future fertility." However, Dr. Fitzgibbons⁴, the author of an accompanying editorial, contends that, there is not yet enough evidence to conclude that using mesh adds to the known fertility risk of hernia repairs, making a change in the informed-consent discussion to include a specific warning about mesh unwarranted. He further notes that these findings are enlightening and certainly provide an invitation for further study.

Causation of inguinal vasal obstruction from the intraoperative use of polypropylene mesh is not conclusively determined. Invasive procedures such as a vasogram would be required to determine the frequency of iatrogenic injury, and these are not always clinically appropriate. An ideal approach to determine incidence would be to perform vasograms in autopsies of patients who had undergone inguinal herniorrhaphy. The authors also note that because reconstruction to restore fertility is extremely difficult when vasal obstruction has occurred, cryopreservation of sperm is recommended at the time of reconstruction.

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3. Shin D, Lipshultz LI, Goldstein M, Barne GA, Fuchs EF, Nagler HM, McCallum SW, Niederberger CS, Schoor RA, Brugh VM 3rd, Honig SC. Herniorrhaphy with polypropylene mesh causing inguinal vasal obstruction: a preventable cause of obstructive azoospermia. *Ann Surg.* 2005;241:553-8.
4. Fitzgibbons RJ Jr. Can we be sure polypropylene mesh causes infertility? *Ann Surg.* 2005;241:559-61.

Kidney Grafts from Living Unrelated Donors: a Preferred Choice in Certain Diseases

Compared to maintenance dialysis, kidney transplantation, a triumph of modern science, has both increased the life expectancy and improved the quality of life in patients with end stage renal disease. Early in the history of kidney transplantation in the United States, a small number of transplants were from living donors who were not related to the recipients. However, by 1970 the use of unrelated donors had stopped. At that

time, the low success rate for the transplantation of organs from genetically unrelated donors did not justify the risk to the donors. Furthermore, the evidence came from early experiments that grafts from one HLA haplotype different donors should be superior in survival to grafts from two HLA haplotype different unrelated donors. The best survival rates were in grafts from HLA-identical siblings.¹ In the clinical kidney transplant experience, for over 20 years, this relationship was assumed to be confirmed because grafts from HLA-identical siblings had the best survival rates, followed by parents, and ultimately cadaver donors.² As the success rate improved with the use of better immunosuppressive drugs, the use of organs from spouses and other "emotionally related" donors, such as close friends, became an accepted practice. The 1995 finding that living unrelated donors (LURDs) yielded survival rates comparable with parental donors³ was surprising and unexpected. This highlighted the additional effect of reperfusion injury in cadaver donor kidneys, which, despite the fact that they were better matched than kidneys from LURDs led to lower graft survival.

Futagawa et al⁴ studied 111,643 first adult kidney transplants from 263 centers using the United Network for Organ Sharing (UNOS) database to describe three diseases; type-I diabetes mellitus, polycystic kidney disease, and focal glomerulosclerosis in which grafts from parental donors had lower survival rates than grafts from LURDs. One possible explanation for these results is that the kidneys from parental donors have some susceptibility to the original disease, making them more vulnerable to damage than kidneys from LURDs. However, when deaths were discounted and functional graft survival was calculated, grafts from parental donors remained lower, and offspring donor grafts had the same survival as LURD, suggesting that lower parental donor graft survival is the result of vulnerability due to age.

In conclusion, LURDs should be given preference over parental and offspring donors for kidney transplantation in patients with focal glomerulosclerosis, polycystic kidney disease or type-I diabetes mellitus.

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Umbilical Cord: an Inexhaustible Source of Blood for Transfusion

Throughout the world, there is always a dire need of fresh blood for transfusion, but its availability is far less than what is required. Dr. Niranjana Bhattacharya¹ addressed this issue by attempting to determine whether fetal hemoglobin-rich placental umbilical cord whole blood could be as a safe substitute for adult whole blood in an emergency. To test this hypothesis, he studied the results of 413 units of placental umbilical cord whole blood transfused into 129 patients (54 men and 75 women; range of age: 2-86 years) at an Indian hospital. Seventy-three patients (57%) suffered from advanced cancer and the rest had other diseases that included ankylosing spondylitis, lupus erythematosus, rheumatoid arthritis, aplastic anemia, and thalassemia major. The blood was collected after cesarean section from consenting mothers and was screened for blood type, syphilis, malaria, HIV, and hepatitis virus. The size of each single unit of transfusion ranged from 50 to 146 mL (average: 86 ± 7.6 mL). No single case of immunologic or nonimmunologic reaction was encountered.

The author concludes that to fulfill the emergency requirements of blood in natural or man-made disaster management, these precious hypimmune fetal cells, which are entrapped inside the placenta, with their altered metabolic profile, are a gift from nature, that could serve as a readily available source of blood in both the under-resourced countries and also in case of a genuine need for blood substitute in a crisis anywhere in the world. Additionally, it also may be safely used for the treatment of malignant and nonmalignant disorders.

It is interesting to note that Goodall et al², back in 1938, reported the use of cord blood for this purpose and deemed it to be "an inexhaustible source of blood for transfusion." However, the report of Boland et al³ that appeared in the following year's *Lancet* that infection was a serious problem brought an end to wide-spread use of this practice.

In recent years, several articles have addressed the use of cord blood units for transplantation in adult and in doing so, have intensified public interest. In 1989, a groundbreaking report of a successful sibling cord blood transplant to a boy with Fanconi anemia was published⁴, which established a new approach to stem cell transplantation. Later, Laughlin et al⁵ showed that allogenic cord blood units trans-

planted into adults showed good outcomes in treatment mortality, degree of graft-versus-host disease, and overall mortality. Rocha et al⁶ reported on transplantation of umbilical cord blood from unrelated donors in adults with acute leukemia. These studies showed that adult patients who need marrow transplants, but who lack a qualified sibling or matched unrelated donor, would do as well with an appropriate cord blood unit transplant as with any marrow donor other than a full six-of-six match.

There are, however, several additional concerns with the use of cord blood, including; the increasing desirability of cord blood as a source of stem cells, problems relating to sterility, and medical-legal issues about whether the mother or the child is the donor. Despite its availability, there are significant problems associated with the use of placental blood for transfusion. Hence, the real challenge remains to make proper rules and regulations that can make this process safe, efficacious and reliable enough for routine use in emergent conditions.

In an editorial published elsewhere, Drs. Snyder and Haley⁷ write: "As we physicians, scientists, health-care providers, and ethicists become wiser with the passage of time, it becomes clear that although the baby is truly to be cherished and loved, there is a good deal to be said for the much maligned bath water as well." All in all, the approach depicted in Dr. Bhattacharya's study further convinces us of the truth of a famous quote by Carl Sandburg that "A baby is God's opinion that life should go on."

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