

SELECTED ABSTRACTS

Getting started with Minimally Invasive Pancreaticoduodenectomy: Is it worth it?

Liang S, Jayaraman S.

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Background

This study evaluates the safety and cost of introducing minimally invasive pancreaticoduodenectomy (MIPD) to a surgeon's practice.

Methods

All MIPDs performed between December 2011 and July 2013 were compared with open pancreaticoduodenectomy (OPD) cases by the same surgeon. The primary outcomes were mortality, major morbidity, and re-operation. Secondary outcomes were perioperative and oncologic outcomes and cost. MIPD include total laparoscopic pancreaticoduodenectomy (TLPD) and laparoscopic-assisted pancreaticoduodenectomy (LAPD), where a small incision is used for reconstruction. Bivariate comparisons of outcomes were performed using nonparametric tests.

Results

In total, 44 pancreaticoduodenectomies were performed: 15 MIPDs (2 TLPDs and 13 LAPDs) and 29 OPDs. One death occurred in each group. Major complication rates were not significantly different (33% for MIPD versus 17% for OPD); however, there was a trend toward more re-operation after MIPD compared with OPD (20% versus 3%; $P=.07$). The incidence of pancreatic leak (20% for MIPD versus 14% for OPD), biliary leak (0% versus 7%, respectively), abscess formation (27% versus 14%, respectively), and intra-abdominal haemorrhage (13% versus 3%, respectively) were not significantly different. MIPD achieved equivalent oncologic outcomes as OPD with 100% R0 margin and adequate lymph node retrieval. There was no statistical difference in median operative time (342 minutes for MIPD versus 358 minutes for OPD), length of stay (8 versus 9 days, respectively), operating room expenses (Canadian) (\$7246.0 versus \$6912.0,

respectively), or total cost (Canadian) per case (\$15,034.0 versus \$18,926.0, respectively).

Conclusions

MIPD and OPD had similar safety and cost in this introductory series. However, a trend toward a higher rate of re-operation for pancreatic leak suggests the need for caution in introducing this novel technique.

Commentary

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This article retrospectively compares pancreaticoduodenectomy performed by laparoscopy; LPD (15 patients) and open surgery (29 patients) by a single surgeon. The number of patients in each group is different and there is no randomization. However, it is clear that in a centre experienced in open pancreaticoduodenectomy shifting to a laparoscopic technique is possible. The shift to laparoscopy may be a sequential pathway with conversions at the beginning. However, whether this shift is of value is not supported by this study. The mortality is one for each group but as a percentage it is 7% for laparoscopy and 3% for open. The major complication rate is mentioned as not significantly different (33% for MIPD versus 17% for OPD), but laparoscopy patients have a higher incidence of intra-abdominal haemorrhage and the re-operation rate is a concern. The oncological outcome and hospital stay are comparable.

A review of eight articles with a total of 492 patients published by Merkow J et al. concludes decreased blood loss, longer operative time, similar post-operative complication rate, decreased pain, and shorter hospital length of stay for LPD. There was also increased number of lymph nodes harvested and similar margin free resections with LPD, favouring LPD.

It is important that the introduction of the laparoscopic technique for pancreaticoduodenectomy should be with caution and not at the expense of patient safety.

Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)

Lancet 2015; 386:1353-61.

Abstract

Summary

Background bisphosphonates have profound effects on bone physiology, and could modify the process of metastasis. We undertook collaborative meta-analyses to clarify the risks and benefits of adjuvant bisphosphonate treatment in breast cancer.

Methods

We sought individual patient data from all unconfounded trials in early breast cancer that randomised between bisphosphonate and control. Primary outcomes were recurrence, distant recurrence, and breast cancer mortality. Primary subgroup investigations were site of first distant recurrence (bone or other), menopausal status (postmenopausal [combining natural and artificial] or not), and bisphosphonate class (amino bisphosphonate [e.g.: zoledronic acid, ibandronate, pamidronate] or other [i.e. clodronate]). Intention-to-treat log-rank methods yielded bisphosphonate versus control first-event rate ratios (RRs).

Findings

We received data on 18,766 women (18,206 [97%] in trials of 2-5 years of bisphosphonate) with median follow-up 5.6 woman-years, 3453 first recurrences, and 2106 subsequent deaths. Overall, the reductions in recurrence (RR 0.94, 95% CI 0.87–1.01; 2p=0.08), distant recurrence (0.92, 0.85–0.99; 2p=0.03), and breast cancer mortality (0.91, 0.83–0.99; 2p=0.04) were of only borderline significance, but the reduction in bone recurrence was more definite (0.83, 0.73–0.94; 2p=0.004). Among premenopausal women, treatment had no apparent effect on any outcome, but among 11,767 postmenopausal women it produced highly significant reductions in recurrence (RR 0.86, 95% CI 0.78–0.94; 2p=0.002), distant recurrence (0.82, 0.74–0.92; 2p=0.0003), bone recurrence (0.72, 0.60–0.86; 2p=0.0002), and breast cancer mortality (0.82, 0.73–0.93; 2p=0.002). Even for bone recurrence,

however, the heterogeneity of benefit was barely significant by menopausal status (2p=0.06 for trend with menopausal status) or age (2p=0.03), and it was non-significant by bisphosphonate class, treatment schedule, oestrogen receptor status, nodes, tumour grade, or concomitant chemotherapy. No differences were seen in non-breast cancer mortality. Bone fractures were reduced (RR 0.85, 95% CI 0.75–0.97; 2p=0.02).

Interpretation

Adjuvant bisphosphonates reduce the rate of breast cancer recurrence in the bone and improves breast cancer survival, but there is a definite benefit only in women who were postmenopausal when treatment began.

Commentary

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Bisphosphonate therapy has long been a mainstay in the treatment of established metastatic bone disease, with multiple beneficial effects including reduction of fracture risk, control of bone pain and treatment of hypocalcaemia. In breast cancer, bisphosphonate therapy has been efficacious in reducing osteoporosis and fracture risk especially in post-menopausal women with ER positive disease.

Recent trials have examined the potential of prophylactic bisphosphonate therapy in reducing breast cancer recurrence in bone, thereby improving survival. Evidence from these have been mixed, with some reports suggesting potential value in early breast cancer although others such as the AZURE trial found no benefit in more advanced disease.

The present paper is a meta-analysis which assesses data from 26 randomized trials involving over 18,000 women with early breast cancer, comparing the use of adjuvant bisphosphonate therapy with controls, looking at local and distant recurrence and overall survival.

The authors report that the data shows highly significant reduction only in bone recurrence, and not in other breast cancer outcomes. They further state that the subgroup analyses suggested benefit in just postmenopausal women, among whom there were

highly significant reductions not only in bone recurrence but also in any distant recurrence and overall survival. The authors speculate that the lack of efficacy seen in pre-menopausal women may be due to the inhibition of bisphosphonate therapy by reproductive hormones.

The results of this analysis have significant implications for the management of early breast cancer in postmenopausal women. Hitherto use of bisphosphonate therapy was restricted to the prevention of bone loss and fractures in such patients treated with aromatase inhibitors. These results suggest an added oncological benefit which may warrant its use in a wider range of patients. In relative terms however this survival benefit may have limited value in a country like Sri Lanka. For example, the pooled data suggest that after 10 years, 14.7 percent of postmenopausal women who used a bisphosphonate died from breast cancer, versus 18.0 percent of women who did not use the drug.

Where adjuvant bisphosphonate therapy have cost implications in a developing country like Sri Lanka, such a small increment in survival may not be adequate to justify widespread use.

Renal tumor biopsy for small renal masses: A single-center 13-year experience

Richard PO, Jewett MA, Bhatt JR, Kachura JR, Evans AJ, Zlotta AR, Hermanns T, Juvet T, Finelli A. *European Urology* 68 (2015) 1007-1013.

Background

Renal tumour biopsy (RTB) for the characterization of small renal masses (SRMs) has not been widely adopted despite reported safety and accuracy. Without pre-treatment biopsy, patients with benign tumours are frequently over treated.

Objective

To assess the diagnostic rate of RTBs, to determine their concordance with surgical pathology, and to assess *their* impact on management.

Design, setting and participants

This is a single-institution retrospective study of 529 patients with biopsied solid SRMs, 4 cm in diameter.

RTBs were performed to aid in clinical management.

Outcome measurements and statistical analysis

Diagnostic and concordance rates were presented using proportions. Factors that contributed to a diagnostic biopsy were identified using a multivariable logistic regression.

Results and limitations: The first biopsy was diagnostic in 90% (n = 476) of cases. Of the non-diagnostic biopsies, 24 patients underwent a second biopsy of which 83% were diagnostic. When both were combined, RTBs yielded an overall diagnostic rate of 94%. Following RTB, treatment could have been avoided in at least 26% of cases because the lesion was benign. Tumour size and exophytic location were significantly associated with biopsy outcome. RTB histology and nuclear grade were highly concordant with final pathology (93% and 94%, respectively). Adverse events were low (8.5%) and were all self-limited with the exception of one. Although excellent concordance between RTB and final pathology was observed, only a subset of patients underwent surgery following biopsy. Thus it is possible that some patients were misdiagnosed.

Conclusions

RTB of SRMs provided a high rate of diagnostic accuracy, and more than a quarter were benign. Routine RTB for SRMs informs treatment decisions and diminishes unnecessary intervention. Our results support its systematic use and suggest that a change in clinical paradigm should be considered.

Commentary

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A renal mass with greatest dimension ≤ 4 cm falls in to the definition of small renal mass (SRMs). Small renal masses account for nearly one-half of all newly diagnosed renal masses, largely based on an incidental diagnosis during widely used abdominal imaging. The incidence of small renal masses is on the rise due to the increased rate of detection. In many series, 30% of small renal masses are of benign histology, hence intervening for all SRMs has a significant risk of overtreatment and

treatment associated complications.

Prediction of histological diagnosis based on clinical features or imaging is not always accurate. On the other hand, renal tumour biopsy is historically poorly accepted mainly due to the fear of tract seeding, poor diagnostic accuracy and biopsy related complications. The debate on the disadvantages and advantages of renal mass biopsy continues despite emerging results supporting the latter. In previous series, the rate of false negative results was considered to be as high as 18%, merely due to the fact that centrally located tumours were not accurately targeted and material obtained in such attempts were not sufficient enough to arrive at a reasonable histological diagnosis. The risk of clinically significant complications of renal tumour biopsy such as perinephric bleeding and pneumothorax are reported to be low (<1%), and needle tract seeding is extremely rare when centrally located, infiltrative renal masses are excluded. Availability and suitability of a wide variety of treatment options ranging from active surveillance and minimally invasive interventions (radiofrequency and cryo-ablation) to surgery for many patients with small renal masses, further highlights the importance of pre-treatment renal mass biopsy in current day practice.

The main drawbacks preventing the recommendation of small renal mass biopsy in routine clinical practice and standard urology guidelines are the paucity of studies with large numbers focusing on the subject, and the sustainability and reproducibility of their results over a sufficient length of time. Therefore the current study with 529 patients over a period of 13 years is of significant value addressing the above mentioned limitations in previous studies.

Long-term results of carmustine wafer implantation for newly diagnosed glioblastomas: a controlled propensity-matched analysis of a French multicenter cohort

Johan Pallud et al.

Neuro Oncol. 2015; 17:1609-19.

Background

The standard of care for newly diagnosed glioblastoma is maximal safe surgical resection, followed by chemoradiation therapy. We assessed carmustine wafer

implantation efficacy and safety when used in combination with standard care.

Methods

Included were adult patients with (n = 354, implantation group) and without (n = 433, standard group) carmustine wafer implantation during first surgical resection followed by chemoradiation standard protocol. Multivariate and case-matched analyses (controlled propensity-matched cohort, 262 pairs of patients) were conducted.

Results

The median progression-free survival was 12.0 months (95% CI: 10.7–12.6) in the implantation group and 10.0 months (9.0–10.0) in the standard group and the median overall survival was 20.4 months (19.0–22.7) and 18.0 months (17.0–19.0), respectively. Carmustine wafer implantation was independently associated with longer progression-free survival in patients with subtotal/total surgical resection in the whole series (adjusted hazard ratio [HR], 0.76 [95% CI: 0.63–0.92], P = .005) and after propensity matching (HR, 0.74 [95% CI: 0.60–0.92], P = .008), whereas no significant difference was found for overall survival (HR, 0.95 [0.80–1.13], P = .574; HR, 1.06 [0.87–1.29], P = .561, respectively). Surgical resection at progression whether alone or combined with carmustine wafer implantation was independently associated with longer overall survival in the whole series (HR, 0.58 [0.44–0.76], P < .0001; HR, 0.54 [0.41–0.70], P < .0001, respectively) and after propensity matching (HR, 0.56 [95% CI: 0.40–0.78], P < .0001; HR, 0.46 [95% CI: 0.33–0.64], P < .0001, respectively). The higher postoperative infection rate in the implantation group did not affect survival.

Conclusions

Carmustine wafer implantation during surgical resection followed by the standard chemoradiation protocol for newly diagnosed glioblastoma in adults resulted in a significant progression-free survival benefit.

Commentary

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The results of this French multicentre study reinforces the significant progression-free survival benefit of carmustine wafers. The wafers are inserted after total/subtotal resection of newly diagnosed glioblastomas and the standard treatment was then implemented. The use of carmustine wafers has not been popular due to the risk of infection being higher and it is reassuring to know that the high postoperative

infection rate in the implantation group did not affect the survival. Extent of surgical resection again proved to be a key independent factor in determining long term progression free survival.

This study raises the question as to whether the use of carmustine wafers should be part of the standard care when treating newly diagnosed glioblastomas.