SELECTED ABSTRACTS

Extending aromatase-inhibitor adjuvant therapy to 10 years
Authors: Goss PE et al. N Engl J Med. 2016;375:209-19

Summary
This phase 3 randomized clinical trial included 1918 postmenopausal women with early breast cancer who had received 5 years of an aromatase inhibitor (AI) either as initial treatment or after any duration of prior tamoxifen. These women were randomised to receive letrozole or placebo for 5 additional years. After a median follow-up of 6.3 years, there were 67 events (disease recurrence or occurrence of contralateral breast cancer) with letrozole and 98 with placebo, and 200 deaths (100 in each group). Extended letrozole treatment was associated with a 34% lower risk of breast cancer recurrence compared with placebo: 5-year DFS rates were 95% and 91%, respectively (HR for disease recurrence or the occurrence of contralateral breast cancer = 0.66, p = 0.01 stratified according to nodal status, adjuvant chemotherapy, the interval from the last dose of AI therapy and the duration of treatment with tamoxifen).

However, the rate of 5-year OS was not significantly different between the groups (93% with letrozole and 94% with placebo; HR=0.97; p=0.83). The annual incidence of contralateral breast cancer was lower in the letrozole group than in the placebo group (0.21% vs. 0.49%; HR 0.42; p=0.007. Bone-related side effects were more frequent with letrozole than with placebo, including a higher incidence of bone pain, fractures and new-onset osteoporosis.

Commentary
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In this trial, women who had completed 5 years of AI therapy were randomised to receive a further 5 years of AI or placebo. Most these women had also received 5 years of tamoxifen. Additional treatment with an AI led to a small decrease in the rate of disease recurrence (including new primary breast cancers) although no difference in OS was reported. Longer duration therapy led to more frequent side effects. These findings are slightly different from ATLAS trial which reported significantly lower recurrences and improved survival with 10-years of extended versus 5-years of tamoxifen.

Conclusion
Extending endocrine therapy for 10 years with AIs may improve DFS but not OS. The decision to continue therapy should be based on individual patient risk stratification.

Treatment of Displaced Mid shaft Clavicle Fractures: Figure-of-Eight Harness Versus Anterior Plate Osteosynthesis: A Randomized Controlled Trial

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Methods

117 patients were randomized into two groups surgical and non- surgical. Non- surgical group was managed with figure of eight harness and surgical group was fixed with antero-inferior plate.

Primary outcome was DASH (Disability of the ARM Shoulder and Hand) Questionnaire at six months. Secondary outcomes included pain, radiographic findings, satisfaction with the cosmetic result, complications, and time to return to previous work and activities. Participants were assessed at 6 weeks, 6 months, and 1 year after the intervention.

Results

No difference between the 2 groups was detected in the DASH score at 6 weeks, 6 months, and 1 year, respectively, pain levels measured with a visual analogue scale (VAS), time to return to previous activities, or dissatisfaction with the cosmetic result. Seven patients (14.9%) developed non-union after non-surgical treatment, a non-union rate that was significantly higher than that in the surgical group, in which all fractures had healed. The patients in the non-surgical group had radiographic evidence of greater clavicle shortening ($p < 0.001$). More patients answered "yes" when asked if they felt paraesthesia in the surgical group

Commentary
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Mid shaft clavicle fractures are common in younger active age group contributing to economy of the country. Over the past decades there has been a debate whether to treat them operatively or conservatively.

Even though traditionally in a developing strained public heath system like Sri Lanka these were treated almost always conservatively there is still a debate whether surgical

treatment would be a better option in displaced mid shaft clavicle fractures. Tamaoki et al has reported a randomised control trial in above providing level-1 evidence in abovementioned article.

Authors concluded that the study did not demonstrate a difference in limb function between patients who underwent surgical treatment and those non-surgically treated for a displaced mid-shaft clavicle fracture. How ever surgical treatment decreased the likelihood of non-union.

This study demonstrates that for displaced mid shaft clavicle fractures non-operative management is still a preferred option even in a high resource setting even more important to a low resource setting like Sri Lanka.

Adjuvant radiotherapy for atypical meningioma's

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Journal of Neurosurgery, June 2017 / Vol. 126 / No. 6: Pages 1822-1828

Abstract

Objective

The aim of this paper was to evaluate outcomes in patients with atypical meningioma's (AMs) treated with surgery alone compared with surgery and radiotherapy at initial diagnosis, or at the time of first recurrence.

Method

Patients with pathologically confirmed AMs treated at the University of Utah from 1991 to 2014 were retrospectively reviewed. Local control (LC), overall survival (OS), Karnofsky Performance Status (KPS), and toxicity were assessed. Outcomes for patients receiving adjuvant radiotherapy were compared with those for patients treated with surgery alone. Kaplan-Meier and the log-rank test for significance were used for LC and OS analyses.

Results

Fifty-nine patients with 63 tumors were reviewed. Fifty-two patients were alive at the time of analysis with a median follow-up of 42 months. LC for all tumors was 57% with a median time to local failure (TTLF) of 48 months. The median TTLF following surgery and radiotherapy was 180 months, compared with 46 months following surgery alone ($p = 0.02$). Excluding Simpson Grade IV (subtotal) resections, there remained an LC benefit with the addition of radiotherapy for Simpson Grade I, II, and III resected tumors (median TTLF 180 months after surgery and radiotherapy compared with 46 months with surgery alone [$p = 0.002$]. Patients treated at first recurrence following any initial therapy (either surgery alone or surgery and adjuvant radiotherapy) had a median TTLF of 26 months compared with 48 months for tumors treated at first diagnosis ($p = 0.007$). There were 2 Grade 3 toxicities and 1 Grade 4 toxicity associated with radiotherapy.

Conclusion

Adjuvant radiotherapy improves LC for AMs. The addition of adjuvant radiotherapy following even a Simpson Grade I, II, or III resection was found to confer an LC benefit. Recurrent disease is difficult to control, underscoring the importance of aggressive initial treatment.

Commentary

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The management of Meningiomas and the controversy of treatment options available has been a long-term point of discussion within the neurosurgical fraternity. Although considered essentially as benign entity the recurrence rate of these tumors is unpredictable and is generally found to be related to the grade of the tumor histologically and the amount resected. A conclusion that is made is that if the tumor is completely resected (Simpson Grade 1) and the meningioma is histological of WHO grade1 that the recurrence rate is extremely low.

This study concluded that there is a definite benefit of lowering local recurrence even in Simpson grade on resections with adjuvant radiotherapy, which is a new concept as prior to this they were under surveillance and only treated if there was a recurrence. This should be carefully considered taking in to account the effects of radiation treatment itself.

Antibiotics Versus Surgical Therapy for Uncomplicated Appendicitis: Systematic Review and Meta-analysis of Controlled Trials (PROSPERO 2015).

Annals of Surgery. 265(5):889–900, MAY 2017

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Abstract

Objective

The aim was to investigate available evidence regarding effectiveness and safety of surgical versus conservative treatment of acute appendicitis.

Summary of background data

There is ongoing debate on the merits of surgical and conservative treatment for acute appendicitis.

Methods

A systematic literature search (Cochrane Library, Medline, Embase) and hand search of retrieved reference lists up to January 2016 was conducted to identify randomized and nonrandomized studies. After critical appraisal, data were analyzed using a random-effects model in a Mantel-Haenszel test or inverse variance to calculate risk ratio (RR) or mean difference (MD) with 95% confidence intervals (CIs).

Results

Four trials and four cohort studies (2551 patients) were included. We found that 26.5% of patients in the conservative group needed appendectomy within 1 year, resulting in treatment effectiveness of 72.6%, significantly lower than the 99.4% in the surgical group, (RR 0.75; 95% CI 0.7-0.79; P = 0.00001; I = 62%). Overall postoperative complications were comparable (RR 0.95; 95% CI 0.35-2.58; P = 0.91; I = 0%), whereas the rate of adverse events (RR 3.18; 95% CI 1.63-6.21; P = 0.0007; I = 1%) and the incidence of complicated appendicitis (RR 2.52; 95% CI 1.17-5.43; P = 0.02; I = 0%) were significantly higher in the antibiotic treatment group. Randomized trials showed significantly longer hospital stay in the antibiotic treatment group (RR 0.3 days; 95% CI 0.07-0.53; P = 0.009; I = 49%).

Conclusions

Although antibiotics may prevent some patients from appendectomies, surgery represents the definitive, one-time only treatment with a well-known risk profile, whereas the long-term impact of antibiotic treatment on patient quality of life and health care costs is unknown. This systematic review and meta-analysis helps physicians and patients in choosing between treatment options depending on whether they are risk averse or risk takers.

Commentary

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Appendicectomy is the commonest non-elective surgical procedure performed around the world. It also remains one of the first major surgeries a trainee performs independently. However, the decision to perform an appendicectomy is not always clear-cut, with the surgeon having to balance the risk of negative appendicectomies vs the risk of perforation. Different approaches have been adopted to minimize negative appendicectomies, like pre-operative CT scanning or the use of laparoscopy. Nevertheless, these too have side effects, complications and costs involved. Therefore, non-operative treatment of acute appendicitis has been attempted, with the use of antibiotics. However, due to the varying quality of the available studies, conclusions have been ambivalent.

This systematic review and meta-analysis by Harnoss et al attempts to address the question on the safety and utility of antibiotic therapy (AT) as an alternative to surgery for acute appendicitis. Their results indicate that during the first 1 year of follow-up, more than one-quarter of the patients undergoing AT required surgery. Furthermore, the patients who did not have surgery were more likely to have adverse effects related to the treatment (RR 3.18, p = 0.0007). Similarly, the risk of complicated appendicitis was doubled in patients treated with antibiotics. The patients who underwent surgery primarily had a shorter primary hospital stay as well.

The main disadvantage for the surgical group was the higher cost ($1140 226 vs $2207 357; P < 0.001). The negative appendicectomy rate was 6%.

Existing data indicate that patients with acute appendicitis in Sri Lanka have a higher chance of undergoing appendicectomy than patients in UK. The surgery is also more likely to be performed as an open procedure and CT is less often used. Despite these practices, the negative appendicectomy rates in Sri Lanka were better than in UK (6.9% vs 20.2%, p=0.003). Therefore, primary surgical management of acute appendicitis may be a better option in Sri Lanka.

References

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