ROUNDUP360

Oncology

Glasgow Prognostic Score in soft-tissue sarcoma

x-ref Research

The high-sensitivity modified Glasgow prognostic score (mGPS) is a prognostic score based on markers of systemic inflammation. It has previously been validated as an excellent marker of survival in various cancers including gastric cancer. The original Glasgow score was based on albumin and CRP, with the modified 'high-sensitivity' variant adding in platelet, leucocyte counts and a high-sensitivity CRP measure. This score has not been used to predict disease-specific survival in soft-tissue sarcoma, and in a relatively simple study design, orthopaedic oncologists in **Tsu-City (Japan)** conducted a prognostic study to establish the value of the score. They retrospectively reviewed the results of 139 patients treated over an 11-year period to establish if the mGPS was of prognostic value.[1] Across the series, the mGPS varied between 0 and 2, and the score appeared to be highly predictive of oncological survival. The chances of survival with an mGPS of 0 were 85.4% at five years, compared with a 0% survival for patients with a score of two. This held true with both disease-specific and event-free survivals across the cohort. To address the issue of confounding effects the research team undertook a multivariant analysis to ensure that the mGPS was an independent risk factor for mortality, and when potential confounders were entered into the model, the mGPS remained an independent predictor of survival.

Denosumab in giant cell tumour

x-ref Research

There are some difficulties associated with unpicking the recent flurry of interest in denosumab. Having become the 'darling' of the oncology world, with highly promising results in RCTs for unresectable or challenging giant cell tumours (GCT), there has been some concern raised by subsequent papers evaluating denosumab in simple GCTs that there may be higher than ideal recurrence rates following cessation of the therapy. The argument again returns to focusing on more challenging tumours, and researchers in **Warsaw (Poland)** have reported their experience of an open label Phase II study focusing on down-staging more advanced GCTs. The study reports the outcomes of 222 patients, all due to undergo surgery for GCT. The research team administered a four-week programme of denosumab therapy. Patients were planned for surgery at commencement of the therapy and differences in planned and actual surgery were reported as part of the study. The study team report a 96% native joint preservation rate in those planned for prosthesis and 86% in those planned for fusion, impressive results in this series despite the complex nature of the GCTs. Of the original 222 patients, at the time of final reporting 48% had not undergone surgery and were still receiving monthly denosumab, while 38% had undergone a lower morbidity procedure than that originally planned.[2] It certainly seems that there is a consistent message emerging in the treatment of complex GCTs: that denosumab can, and consistently does, down-stage lesions and can result in either no subsequent requirement for surgery or requirement for a lower morbidity procedure.

Timing, complications and radiotherapy

Radiotherapy is a useful adjunct in the treatment of soft-tissue sarcoma. While this offers the potential for improved survival when given as a pre-operative adjunct, on the other hand there is an increased risk of difficulties associated with wound healing complications. As yet there is little data to support surgical decision making surrounding the timing of radiotherapy and surgery to minimise wound-healing problems. A study team in **Ontario (Canada)** set out to establish any potential association between the two. Their study reported the retrospective outcomes of nearly 800 patients, all having had pre-operative radiotherapy and then surgery at different timings. Outcomes were reported in terms of wound complications requiring a secondary procedure, VAC closure or prolonged dressing changes.[3] The cohort had a mean tumour size of 8.8 cm and the overwhelming majority (93%) were primary presentations. The surgeons here report a wound complication rate of 30% (n = 242), with the majority of the problems presenting in lower limb tumours (85%). The authors could not find any temporal association with surgical timing and complication occurrence. Even with careful subgroup and secondary analyses, the wound complication rates were apparently only minimally affected by surgical window.

Pigmented villonodular synovitis and arthroscopy

x-ref Knee

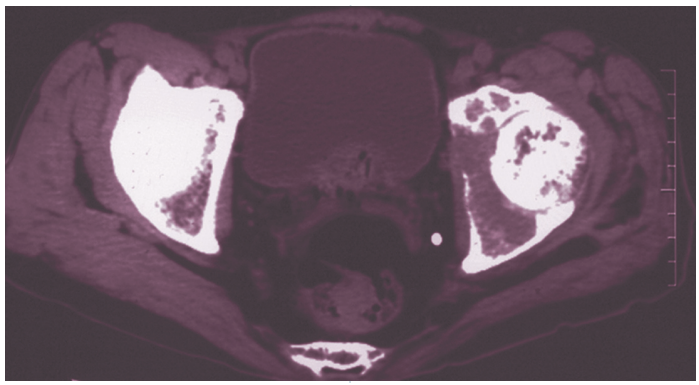
Pigmented villonodular synovitis (PVNS) is a so-called 'borderline malignant' condition. Presenting often with knee pain and swelling and insidious symptom onset, PVNS is managed often in knee clinics; there is some disparity in opinion about how it should be best managed. Historically, in view of the malignant potential of this condition, PVNS has been managed by extensive open debridement. However, this carries with it a significant morbidity, and more recently surgeons have been attempting arthroscopic debridement. Opinion is mixed as to which approach represents the most effective way of managing the condition, although there is much published on the relative outcomes – an ideal

situation for a meta-analysis such as that reported by colleagues in **Ontario (Canada)**. The review team identified 35 trials that were suitable for inclusion in the study and were able to include the aggregated results of 630 patients in their meta-analysis. There was a surprisingly high incidence of recurrence following surgery, with around 1:5 patients requiring revision surgery. The key predictor of recurrence in this paper was the type of surgery. Open surgery alone had a lower risk of recurrence over arthroscopic surgery in DPVNS (odds ratio 0.47), which was significantly improved by combining open and arthroscopic procedures (OR 0.19). This was not the case with the localised PVNS and there were no signs of radiotherapy to help matters either.[4] The 'take-home' message from this study is that arthroscopic surgery alone is less effective than open synovectomy with or without arthroscopic assistance in PVNS. Although a larger procedure, the chances of cure are better with a proper excision!

PATHFx: estimating survival in pathological cancer

x-ref Research

■ Estimating survival in patients with pathologic fracture is a tricky thing to do. There are a number of 'survival estimate' papers in the literature and they all revolve around a variety of regression analysis models designed to use covariate risk factors to give an estimated survival. We would agree here at *360* with the basic premise of all of these papers, that estimating survival is helpful in making treatment decisions; the difficulty has always been application of complex logistic regression models. We were heartened to read a new paper from **Rome (Italy)** which tries to validate the tried and tested methodology of multivariant analysis to estimate survival of a given patient using prognostic data. The PathFx tool was previously developed using a Bayesian Belief Network and data from 189 patients.



The study group have recently produced a web-based tool (www.pathfx.org) with the aim of making estimation of survival easier. This current paper concerns validation of the model using data from 287 patients presenting with pathological fractures. Using a ROC method to establish the sensitivity and specificity of the model, an AUC of 0.80 for three months' survival and 0.77 for 12 months' survival (representing excellent prognostic value) was reported in this study.[5] PATHFx may well become a definitive tool. The website provides a clear and easy to use prognostic tool with the ability to accurately estimate survivals. We are delighted to see such an easy to use application of a form of multivariant model.

Prosthetic lengthening of short stumps

x-ref Trauma

■ In high hip amputation there is sometimes no option but to perform a hip disarticulation. If the residual stump is too short, the patient is unable to ambulate without prosthesis, and the residual stump suffers from poor control. It is not uncommon following either tumour resection or trauma for the residual stump to be disappointingly short. This then potentially causes the issue that a prosthesis cannot be worn and the patient may be better with a hip disarticulation.[6] Surgeons in **Münster (Germany)** have reported their experience with prosthetic stump lengthening procedures which offer patients the potential to preserve a functioning stump rather than resulting in disarticulation. Due to the rarity of this condition, the authors report the results of 28 patients, all of whom underwent stump lengthening procedures with a modular tumour endoprosthesis. As perhaps might be expected, the complication rates were rather high - just over 50% of patients suffered complications to their treatment, with infection being the most common problem. This said, over 90% of patients were able to use a prosthetic limb at final follow-up and the mean Musculoskeletal Tumour Society Score was 56% (n = 11). It certainly seems from this small series that use of a modular endoprosthesis for stump lengthening is a valuable technique resulting in acceptable functional outcomes from a very poor preoperative condition.

Chondrosarcoma and pathological fracture

■ It is well known that pathological fracture in osteosarcoma increases the risks of limb salvage surgery (presumably due to localised seeding of cancer cells) but that in the longer term it does not greatly affect survival. Fracture, however, is far from benign and, if at all possible, should be avoided. Surgeons in **Buenos Aires (Argentina)** have drawn together their own experience of pathological fracture of the femur in a large cohort of 182 patients. This study looks at chondrosarcoma at just one site (femur) and examines a number of prognostic factors. The study authors examine the prognostic value of patient demographics, chondrosarcoma grade and other surgery-related factors.[7] In their series, the overall disease-free survival rate was 69% at five years, although this was significantly lower in the fracture group (49%). This was mostly due to the poorer outcomes in patients with grade I chondrosarcomas. In addition to this, fracture was seen in this group to increase the risk of local recurrence in dedifferentiated chondrosarcoma. All in all, there is a fairly clear message here – treatment before fracture is definitely preferred.

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