

## Managing patients with advanced cancer: the benefits of early referral for palliative care

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*Palliative care is becoming fundamental in the starting line-up of care choices*

For Australian patients with advanced, incurable illness, particularly cancer, the option of referral to specialist palliative care services can seem to be a random and discretionary default option that is sometimes called on when all possibilities for life-extending treatment have been exhausted or cannot easily be accessed. Palliative care services (distinct from palliative chemotherapy) provide a broad range of inputs to patients and their carers and loved ones, including specialised medical and nursing management and advice on symptom control; psychological, emotional and spiritual support; practical nursing care; advice and assistance with goal setting and end-of-life care; and bereavement counselling and support. Despite offering these and other unique strategies in the field of cancer management, these specialist palliative care services sometimes stay on the substitute's bench until called on late, when all else has failed.

In Australia, despite having had principles of goal setting and broad palliative care education as part of the medical curriculum for over 20 years,<sup>1-3</sup> and despite evidence of the benefits of referral to specialist palliative care services,<sup>4</sup> only 42% of patients who die of advanced cancer and other terminal illnesses in the country's busiest acute hospital are referred to a specialist palliative care service.<sup>5</sup> Patients with haematological malignancies are referred less frequently than patients with solid tumours.<sup>6</sup> Although oncologists in Australia report that they favour early referral for specialist palliative care, with a concurrent rather than sequential model of care,<sup>7</sup> patients are usually referred late. In one large, integrated Australian palliative care service, patients had a median length of survival after referral of 54 days, representing the final 17% of their illness duration.<sup>8</sup>

Perceived barriers to improving palliative care referral and provision include inadequate communication about goal setting and resuscitation orders; inadequate symptom control; and lack of resources, including inadequate bereavement counselling of care-givers.<sup>7</sup> A Queensland senator recently called Australian palliative care services "an under-resourced shambles".<sup>9</sup>

In Australia and elsewhere, there have been increasing efforts to more accurately define the benefits or otherwise of early referral to palliative care services for patients with an incurable and progressive illness. However, research has been difficult, and randomised controlled trials have not been of high impact.

Now, the results of two recent prospective, randomised studies from the United States<sup>10,11</sup> will help to broaden Australian clinicians' and the public's understanding of the role of specialist palliative care services in the care of patients with advanced, incurable cancer and the advantages of early referral. Although the evidence from these studies has limited application in Australia because of differences in the US and Australian health care systems, the models of care being tested are similar to current Australian models, and the results have the potential to significantly shape practice and policy in this increasingly important part of health care.<sup>9</sup>

A non-blinded randomised controlled trial reported by Temel and colleagues<sup>10</sup> provides a watershed moment in oncology and palliative

care. One hundred and fifty-one ambulatory patients referred to an outpatient thoracic oncology clinic for newly diagnosed non-small cell metastatic lung cancer were randomly allocated to standard oncology care with or without referral to a palliative care team. The primary outcome was change in health-related quality of life at 12 weeks. Patients in the early palliative care group had better quality of life and fewer depressive symptoms compared with those receiving only standard care (Box).

The various goals of new interventions in cancer treatment include improving survival; reducing treatment toxicity; improving quality-of-life scores (eg, mood); and reducing the financial costs of treatment. This study achieved all these goals with just the modest intervention of an average of four visits from the specialist palliative care team in the first 12 weeks.

Importantly, the median survival time of 8.9 months was at least as good as would be predicted and expected for the control group. The improvement in overall survival of 2.7 months (30%) for the intervention group who were referred for early palliative care was equal to or greater than that achieved for comparable patient groups with chemotherapy versus best supportive care<sup>12</sup> or the addition of the new and very expensive targeted agents cetuximab or bevacizumab to chemotherapy.<sup>13,14</sup> It was achieved despite significantly fewer patients receiving aggressive end-of-life care. The size of the survival benefit may have been reduced because 14% of the control group also received early referral to a specialist palliative care service for symptom control and had 1–2 palliative care visits during the 12 weeks. A survival advantage from early palliative care referral has been suggested previously,<sup>15</sup> but will need to be replicated by studies in other care settings and in patients with other types of cancer.

Possible weaknesses of this study are the lack of blinding and lack of patient comorbidity data. Extra time spent with health care professionals, rather than any specific palliative care intervention, may have contributed to the improvements seen. But if this were so, this effect would also have been expected in studies showing benefits of chemotherapy plus best supportive care versus best supportive care alone, whereas no difference was shown in survival advantage between these groups.<sup>12</sup> Also, even though the patient groups were balanced for types of chemotherapy and other treatments at enrolment and for the number of courses of chemotherapy during the study, more detailed data on specific chemotherapy regimens are lacking.

Wright and colleagues<sup>11</sup> followed 333 patients with advanced cancer from their enrolment until their death. Those referred to specialist palliative care services had better outcomes when treated outside an acute hospital (Box). Assessment of their carers at enrolment and after the death of the patient showed that those who were assisted in providing care at home until the patient's death had significantly less risk of developing post-traumatic stress disorder or prolonged grief disorder.

In the future, as we seek to confirm and understand more about how these improvements were achieved in patients receiving specialist palliative care, early referral for palliative care should

**Two recent US studies showing benefits of early specialist palliative care in patients with advanced cancer: overview**

Temel et al<sup>10</sup>

**Research question:** Does early referral of ambulatory patients with newly diagnosed metastatic non-small cell lung cancer to a specialist palliative care service affect patient-reported outcomes, use of health services and quality of end-of-life care?

**Design**

- Non-blinded randomised controlled trial; 151 lung cancer patients referred to an outpatient clinic
- Standard oncology care versus standard care with referral to a palliative care team (seen within 3 weeks, and at least monthly until death)
- Groups well balanced for all known prognostic factors, initial cancer therapy, and baseline quality of life and mood
- Quality of life and mood assessed at baseline and 12 weeks
- Data on end-of-life care derived from medical records

**Findings**

- Patients assigned to early palliative care received an average of four palliative care visits in 12 weeks (range, 0–8 visits)
- Patients in the intervention group had better quality of life than patients assigned to standard care
- Proportion of patients with clinical depression decreased in the intervention group from 22% to 16% and increased in the control group from 25% to 38% ( $P=0.01$ )
- Fewer patients with early palliative care compared with standard care received aggressive end-of-life care (33% v 54% of those who had died by time of analysis;  $P=0.05$ ). Median survival was significantly longer among patients receiving early palliative care (11.6 v 8.9 months;  $P=0.02$ )

Wright et al<sup>11</sup>

**Research question:** Is the place of death for patients with cancer associated with patients' quality of life at the end of life and psychiatric disorders in bereaved caregivers?

**Design**

- Prospective, longitudinal multisite study; 333 patients with advanced cancer and their caregivers
- Patients followed from enrolment to death (median, 4.5 months)
- Quality of life at end of life assessed by caregiver report within 2 weeks of death
- Caregivers' mental health assessed at baseline, and 6 months after patient's death

**Findings**

- Patients who died in an intensive care unit or hospital experienced more physical and emotional distress and worse quality of life at the end of life compared with patients who died at home with palliative care
- Death in an intensive care unit was associated with a greater risk of post-traumatic stress disorder in carers compared with death at home with palliative care (21.1% v 4.4%;  $P=0.02$ )
- Death in hospital was associated with heightened risk for prolonged grief disorder in carers compared with death at home with palliative care (21.6% v 5.2%;  $P=0.02$ ) ◆

care services in the care of patients with advanced, incurable cancer. They show that early referral can improve all measurable outcomes for patients by as much as, or more than, new and expensive treatments. Further, they show that early referral can help patients and carers better understand and choose between their treatment options near the end of life, reducing futile use of finite medical resources, debilitating treatments such as continuing cycles of chemotherapy in very advanced stages of illness, and acute in-hospital interventions at the end of life. The incidence of subsequent emotionally and financially debilitating psychological and psychiatric sequelae in the carers of these patients can be reduced. Because of new high-quality evidence, palliative care is rapidly moving from being an ancillary and sometimes discretionary medical treatment option to being fundamental in the starting line-up of care choices for patients with advanced cancer. If early referral for specialist palliative care were an expensive new drug, it would quite appropriately be marketed as a major advance in improving the care of patients with incurable cancer.

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become part of all arms of any randomised trial of advanced cancer treatment, particularly when a new treatment is being compared with best supportive care or current best treatment.

The results of the two studies discussed here provide the best evidence yet for the multiple benefits of early referral to palliative