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LETTER TO THE EDITOR

EMOTIONAL DISTRESS – A NEGLECTED TOPIC AMONG SURGICALLY TREATED OESOPHAGEAL CANCER PATIENTS

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INTRODUCTION

Oesophageal cancer is the 8th most common type of cancer in the world and the 6th most common cancer-related cause of death. Age of onset is most commonly between 65 and 70 years, with a strong male predominance (2–4:1 male to female).^[1] Oesophageal cancer has two main histological types with different causes and patterns of incidence; adenocarcinoma and squamous cell carcinoma. The incidence of adenocarcinoma has increased rapidly over the past decade, now having surpassed the incidence of squamous cell carcinoma.^[2] The main risk factors for adenocarcinoma of the oesophagus are obesity, gastro-oesophageal reflux disease, Barrett's oesophagus and being male, whereas smoking and high alcohol consumption are the main risk factors for squamous cell carcinoma.^[3]

Due to the expandable nature of the oesophagus, a tumour may remain undetected for some time. Consequently oesophageal cancer is often diagnosed at a late stage and the prognosis is very poor, with an overall 5-year survival of 10% in Europe.^[4] The most established curatively intended treatment to date involves extensive surgical resection; oesophagectomy with eradication of local and regional lymph nodes, either via a transthoracic or a transhiatal approach, often in combination with neoadjuvant therapy.^[5-7] However, only approximately 25% of patients are eligible for potentially curative surgery as the remaining have more advanced disease, poor fitness and pre-existing co-morbidities.^[8] The surgery is more extensive than any other standard surgical procedure, and up to half of all patients experience severe post-operative complications that typically require a long convalescence period and severely impact health-related quality of life (HRQL) in the long-term.^[9-11] The prognosis is unfavourable even when the tumour is surgically removed, with a post-operative 5-year survival rate of 31%.^[8]

CURRENT POSITION

Oesophageal cancer patients experience not only serious physical consequences of their disease and treatment but also substantial psychological trauma. Although one third of all cancer patients are estimated to suffer from some type of psychiatric disorder during active treatment,^[12] most research to date investigating oesophageal cancer patients' recovery following surgery has focused largely on impaired functions and symptoms experienced. Previous studies show that patients suffer greatly reduced HRQL as a consequence of the disease and treatment, both in the short- and long-term.^[13] Among long-term survivors, the majority of patients recover in terms of HRQL to a level comparable with the background population within 3 to 5 years.^[14] However, for a minority of long-term survivors, symptoms and functions remain impaired or deteriorate even further.^[15] Emotional function is one HRQL domain that appear to improve over time,^[16, 17] particularly among elderly patients.^[18] Interestingly, one study found that an improvement in emotional functioning from the time of oesophageal cancer diagnosis to 6 months post-treatment was associated with better survival.^[17]

Surprisingly few studies have investigated emotional adjustment more specifically among surgically treated oesophageal cancer patients. The prevalence of depression was 27% in a longitudinal study including both oesophageal and gastro-oesophageal junction cancer patients without a history of psychiatric illness.^[19] Depression was assessed using the Hospital Anxiety and Depression Scale (HADS) following oesophageal cancer diagnosis, but prior to treatment decision. The depression prevalence was lower among patients who were subsequently treated with curative intent (21%) than among the palliative patients (46%). A non-significant trend was observed for an increase in the prevalence of depression over 6 months in this study. Depression was unrelated to patient characteristics or clinical factors, including treatment regime, however greater functional

impairment was associated with elevated depression symptoms. Using the HADS, similar prevalence rates of depression have been observed in other studies including surgically treated oesophageal cancer patients only. One recent study found that 24% of patients reported depression at a median 45 months following diagnosis, and those patients who reported co-morbidities were also more likely to be depressed.^[20] Further, one longitudinal study of 189 surgically treated oesophageal cancer survivors at a median time of 48 months following diagnosis, reported that depressive symptoms appear to persist or even increase over time. None of the depressed patients reported an improvement in depressive symptoms over a 12-month period in this study.^[21]

Anxiety, like depression, is more frequent among cancer patients than in the general population but its incidence varies according to age, sex, type of cancer, tumour stage, course of treatment, and time in relation to diagnosis.^[22, 23] However, anxiety among oesophageal cancer patients following surgical resection has been poorly investigated. The prevalence of anxiety was 36% in a sample of surgically treated oesophageal cancer patients 4 years following diagnosis. Younger patients and patients who reported not having a carer were more likely to be anxious.^[20] There is also evidence that anxiety symptoms may increase over time. One study assessing change in anxiety over time, in a sample of early stage oesophageal cancer patients following surgical treatment, found that the majority (55%) of patients shifted from reporting no anxiety at study inclusion (median time 45 months post diagnosis) to reporting elevated anxiety based on HADS criteria for a probable anxiety disorder one year later.^[21] Findings from one longitudinal study showed that in contrast to depression, which was most elevated during treatment, anxiety was greatest at the time of diagnosis, but decreased over time in a mixed sample of palliative and curatively treated oesophageal cancer patients.^[19] In this study, the prevalence of anxiety, as measured by the HADS, ranged from 16% to 34% over a 12-month period. Following an initial decrease in

anxiety, a spike in symptoms was observed at 3 months following inclusion in the study, for patients treated with curative intent, with rates once again similar to those reported at inclusion. Duration of tumour-related symptoms experienced before oesophageal cancer diagnosis was associated with elevated anxiety scores at time of inclusion, and female patients were more anxious than male patients. Not surprisingly, anxiety strongly co-varied with depression. The majority of depressed patients also reported anxiety symptoms (73%) above the clinical threshold.

Some studies also suggest that emotional distress among surgically treated oesophageal cancer patients may be influenced by patients' illness perceptions. Illness perceptions refer to the cognitive models and explanations an individual has regarding their illness or health condition.^[24] Few studies have investigated the role of patients' illness perceptions on subsequent emotional distress, but the limited available evidence suggests that patients who perceive greater consequences from their condition and report a poorer understanding of their cancer, also experience greater anxiety and depression 4 years post-diagnosis.^[20] In this study, patients with stronger perceptions of disease controllability reported reduced depression symptoms. Both anxiety and depression symptoms were elevated when patients perceived the cause of their illness to be emotional (e.g. stress or worry), but decreased if the cause was perceived to be external (e.g. hereditary or a virus). Weaker perceptions over time in terms of personal and treatment control over the cancer were associated with significantly increased anxiety and depression symptoms over a 12-month period, independent of a range of demographic and clinical variables. Additionally, patient anxiety was also influenced by the illness perceptions of the spouses. In particular, stronger perceptions of greater consequences of the cancer among spouses were associated with increased patient anxiety. Poorer understanding of the cancer increased depression in the patients, but even more so when the spouse perceived that the patient's understanding of the

cancer was high.^[25] One study of psychological distress among carers of oesophageal cancer patients found moderate to severe levels of anxiety (19% and 11%, respectively) and depression (8% and 2%, respectively) among carers 46 months following the patient's diagnosis. Psychological distress was lower when the carers more strongly believed that they understood the patient's condition, or more strongly believed that the oesophageal cancer patient's condition could be controlled by treatment or the patient's own behaviour.^[26]

FUTURE DIRECTIONS

It is clear that emotional distress, as a consequence of oesophageal cancer, has received little attention to date. Although limited, the available evidence suggests that oesophageal cancer patients experience significant levels of distress both in the short- and long-term. Taken together, the proportion of patients reporting anxiety and depression ranges from 24% to 64% across studies, and results suggest that greater functional impairment, co-morbidities, a poorer understanding of the cancer, and a perception of greater consequences of the oesophageal cancer on patients' lives are factors associated with depressed mood, whereas perceptions of greater control are associated with lower levels of depressed mood. Anxiety is associated with younger age, female gender, the absence of a carer, longer duration of pre-diagnosis tumour-related symptoms, a poorer understanding of the illness and a perception of greater consequences of the cancer. There is also an indication of different trajectories for depression and anxiety symptoms, where the former appears more common during the treatment phase and the latter at the time of diagnosis. Illness perceptions held by spouses of oesophageal cancer patients are also associated with patient distress, suggesting that in order to fully understand the emotional consequences of oesophageal cancer, the role of the patient's carer, most often the spouse, should also be taken into account. It is, however,

difficult to draw conclusions from the literature due to the predominantly cross-sectional designs, the varying assessment times, the small sample sizes, the poor response rates, and the presentation of results from combined samples of palliative patients and patients treated with curative intent. Further, although the majority of studies used HADS, the most extensively validated scale for screening emotional distress in cancer patients, it is important to note that the clinical thresholds for anxiety or depression varies across studies, influencing diagnostic accuracy.^[27]

In conclusion, there is a clear and substantial need for well-designed, prospective, nationwide population-based, representative studies on the emotional distress experienced by oesophageal cancer patients following surgical treatment in order to 1) establish the prevalence of emotional distress, 2) identify the risk factors for poor emotional adjustment following treatment and to establish the impact on recovery, and 3) clarify the role of patients' carers on emotional distress among patients. To reduce the suffering among these patients, further research on the emotional consequences of oesophageal cancer is highly warranted.

CONFLICTS OF INTEREST STATEMENT

The authors declare that no conflicts of interest exist.

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REFERENCES

1. Ferlay J, Shin HR, Bray F, et al: Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Can* 2010; 127: 2893-2917.
2. Cook MB, Chow WH, Devesa SS: Oesophageal cancer incidence in the United States by race, sex, and histologic type, 1977-2005. *Br J Cancer* 2009; 101: 855-859.
3. Enzinger PC, Mayer RJ: Esophageal cancer. *N Engl J Med* 2003; 23: 2241-2252.
4. Parkin DM, Bray F, Ferlay J, Pisani P: Global cancer statistics, 2002. *CA Cancer J Clin* 2005; 55: 74-108.
5. Wu PC, Posner MC: The role of surgery in the management of oesophageal cancer. *Lancet Oncol* 2003; 4: 481-488.
6. Sjöquist KM, Burmeister BH, Smithers BM, Zalcberg JR, Simes RJ, Barbour A, et al: Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. *Lancet Oncol* 2011; 12: 681-692.
7. van Hagen P, Hulshof MC, van Lanschot JJ, Steyerberg EW, van Berge Henegouwen MI, Wijnhoven BP, et al: Preoperative Chemoradiotherapy for Esophageal or Junctional Cancer. *N Engl J Med* 2012; 366: 2074-2084.
8. Rouvelas I, Zeng W, Lindblad M, Viklund P, Ye W, Lagergren J: Survival after surgery for oesophageal cancer: a population-based study. *Lancet Oncol* 2005; 6: 864-870.

9. Viklund P, Lindblad M, Lu M, Ye W, Johansson J, Lagergren J: Risk factors for complications after esophageal cancer resection: a prospective population-based study in Sweden. *Ann Surg* 2006; 243: 204-211.
10. Daly JM, Fry WA, Little AG, Winchester DP, McKee RF, Stewart AK, et al: Esophageal cancer: results of an American College of Surgeons patient care evaluation study. *J Am Coll Surg* 2000; 190: 562-572.
11. Derogar M, Orsini N, Sadr-Azodi O, Lagergren P: Influence of major postoperative complications on health-related quality of life among long-term survivors of esophageal cancer surgery. *J Clin Oncol* 2012; 30:1615-1619.
12. Singer S, Das-Munshi J, Brähler E: Prevalence of mental health conditions in cancer patients in acute care: a meta-analysis. *Ann Oncol* 2010; 21: 925-930.
13. Djärv T, Lagergren P: Quality of life after esophagectomy for cancer. *Expert Rev Gastroenterol Hepatol* 2012; 6: 115-122.
14. Djärv T, Lagergren J, Blazeby JM, Lagergren P: Long-term health-related quality of life following surgery for oesophageal cancer. *Br J Surg* 2008; 95: 1121-1126.
15. Derogar M, Lagergren P: Health-related quality of life among 5-year survivors of esophageal cancer surgery: a prospective population-based study. *J Clin Oncol* 2012; 30: 413-418.
16. Lagergren P, Avery KN, Hughes R, Barnham CP, Alderson D, Falk SJ, et al: Health-related quality of life among patients cured by surgery for esophageal cancer. *Cancer* 2007; 110: 686-693.

17. Blazeby JM, Brookes ST, Alderson D: The prognostic value of quality of life scores during treatment for oesophageal cancer. *Gut* 2001; 49: 227-230.
18. Parameswaran R, McNair A, Avery KN, Berrisford RG, Wajed SA, Sprangers MA, et al: The role of health-related quality of life outcomes in clinical decision making in surgery for esophageal cancer: a systematic review. *Ann Surg Oncol* 2008; 15: 2372-2379.
19. Bergquist H, Ruth M, Hammerlid E: Psychiatric morbidity among patients with cancer of the esophagus or the gastro-esophageal junction: a prospective, longitudinal evaluation. *Dis Esophagus* 2007; 20: 523-529.
20. Dempster M, McCorry NK, Brennan E, Donnelly M, Murray L, Johnston BT: Psychological distress among survivors of esophageal cancer: the role of illness cognitions and coping. *Dis Esophagus* 2012; 25: 222-227.
21. Dempster M, McCorry NK, Brennan E, Donnelly M, Murray L, Johnston BT: Do changes in illness perceptions predict changes in psychological distress among oesophageal cancer survivors? *J Health Psychol* 2011; 16: 500-509.
22. Linden W, Vodermaier A, Mackenzie R, Mackenzie R, Greig D: Anxiety and depression after cancer diagnosis: Prevalence rates by cancer type, gender, and age. *J Affect Disord* 2012; 141: 343-351.
23. Hinz A, Krauss O, Hauss JP, Höckel M, Kortmann RD, Stolzenburg JU, et al: Anxiety and depression in cancer patients compared with the general population. *Eur J Can Care* 2010; 19: 522-529.

24. Leventhal H, Meyer D, Nerenz DR: The common sense representation of illness danger. In *Contributions to Medical Psychology*, Vol 2, Rachman S (ed). Pergamon Press: New York, 2012; 17-30
25. Dempster M, McCorry NK, Brennan E, Donnelly M, Murray L, Johnston BT: Illness perceptions among carer-survivor dyads are related to psychological distress among oesophageal cancer survivors. *J Psychosom Res* 2011; 70: 432-439.
26. Dempster M, McCorry NK, Brennan E, Donnelly M, Murray L, Johnston BT: Psychological distress among family carers of oesophageal cancer survivors: the role of illness cognitions and coping. *Psycho-Oncology* 2011; 20:698-705.
27. Vodermaier A, Millman RD: Accuracy of the Hospital Anxiety and Depression Scale as a screening tool in cancer patients: a systematic review and meta-analysis. *Support Care Cancer* 2011; 19:1899-1908.