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[Intervention Review]

Palliative chemotherapy and targeted therapies for esophageal and gastroesophageal junction cancer

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ABSTRACT

Background

Almost half of people with esophageal or gastroesophageal junction cancer have metastatic disease at the time of diagnosis. Chemotherapy and targeted therapies are increasingly used with a palliative intent to control tumor growth, improve quality of life, and prolong survival. To date, and with the exception of ramucirumab, evidence for the efficacy of palliative treatments for esophageal and gastroesophageal cancer is lacking.

Objectives

To assess the effects of cytostatic or targeted therapy for treating esophageal or gastroesophageal junction cancer with palliative intent.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, the Web of Science, PubMed Publisher, Google Scholar, and trial registries up to 13 May 2015, and we handsearched the reference lists of studies. We did not restrict the search to publications in English. Additional searches were run in September 2017 prior to publication, and they are listed in the 'Studies awaiting assessment' section.

Selection criteria

We included randomized controlled trials (RCTs) on palliative chemotherapy and/or targeted therapy versus best supportive care or control in people with esophageal or gastroesophageal junction cancer.

Data collection and analysis

Two authors independently extracted data. We assessed the quality and risk of bias of eligible studies according to the *Cochrane Handbook for Systematic Reviews of Interventions*. We calculated pooled estimates of effect using an inverse variance random-effects model for meta-analysis.

Main results

We identified 41 RCTs with 11,853 participants for inclusion in the review as well as 49 ongoing studies. For the main comparison of adding a cytostatic and/or targeted agent to a control arm, we included 11 studies with 1347 participants. This analysis demonstrated an

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increase in overall survival in favor of the arm with an additional cytostatic or targeted therapeutic agent with a hazard ratio (HR) of 0.75 (95% confidence interval (CI) 0.68 to 0.84, high-quality evidence). The median increased survival time was one month. Five studies in 750 participants contributed data to the comparison of palliative therapy versus best supportive care. We found a benefit in overall survival in favor of the group receiving palliative chemotherapy and/or targeted therapy compared to best supportive care (HR 0.81, 95% CI 0.71 to 0.92, high-quality evidence). Subcomparisons including only people receiving second-line therapies, chemotherapies, targeted therapies, adenocarcinomas, and squamous cell carcinomas all showed a similar benefit. The only individual agent that more than one study found to improve both overall survival and progression-free survival was ramucirumab. Palliative chemotherapy and/or targeted therapy increased the frequency of grade 3 or higher treatment-related toxicity. However, treatment-related deaths did not occur more frequently. Quality of life often improved in the arm with an additional agent.

Authors' conclusions

People who receive more chemotherapeutic or targeted therapeutic agents have an increased overall survival compared to people who receive less. These agents, administered as both first-line or second-line treatments, also led to better overall survival than best supportive care. With the exception of ramucirumab, it remains unclear which other individual agents cause the survival benefit. Although treatment-associated toxicities of grade 3 or more occurred more frequently in arms with an additional chemotherapy or targeted therapy agent, there is no evidence that palliative chemotherapy and/or targeted therapy decrease quality of life. Based on this meta-analysis, palliative chemotherapy and/or targeted therapy can be considered standard care for esophageal and gastroesophageal junction carcinoma.

PLAIN LANGUAGE SUMMARY

Palliative (without intention to cure) chemotherapy and targeted therapies for cancer in the esophagus or gastroesophageal junction

Review question

This review aimed to investigate the effectiveness of adding cytostatic or targeted therapy to supportive care in people with esophageal or gastroesophageal junction cancer.

Background

Esophageal cancer is the eighth most common cancer in the world. Many people are diagnosed only after the disease has spread to other parts of the body, when cure is rarely possible. These people can be treated with palliative chemotherapy or targeted therapy (a drug directed against a specific component of the tumor). The aim of this treatment is to control tumor growth and increase survival, without a significant decrease in quality of life.

Study characteristics

We searched reference lists, biomedical databases (Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, the Web of Science, PubMed Publsiher, and Google Scholar), and trial registries up to 13 May 2015. Additional searches were run in September 2017 prior to publication, and they are listed in the 'Studies awaiting assessment' section.

Key results

We identified 41 randomized controlled trials (RCTs) that met our inclusion criteria for inclusion in the review, as well as 49 ongoing studies. This review and meta-analysis shows that people who receive more chemotherapeutic or targeted therapeutic agents live longer and with less disease progression than people who receive best supportive care or less therapy. The only individual agent that more than one study found to improve survival was ramucirumab. We found severe treatment-associated toxicities (grade 3 or above) more frequently in the arms with an additional chemotherapy or targeted therapy agent. However, there is no evidence that palliative chemotherapy and/or targeted therapy decreases quality of life. Our meta-analysis indicates that chemotherapy and targeted therapy are effective palliative treatments for people with esophageal and gastroesophageal junction cancer.

Quality of the evidence

The evidence that more chemotherapeutic or targeted therapeutic agents increase survival is of high quality, as is the evidence for improved survival compared to best supportive care. The evidence for the increased occurrence of severe treatment-related toxicities is of very low quality, while the evidence showing no decrease in quality of life is also low quality.

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