Peri-operative Outcomes and Survival Following Palliative Gastrectomy for Gastric Cancer: a Systematic Review and Meta-analysis

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Accepted: 9 September 2020 / Published online: 22 September 2020 © The Author(s) 2020

Abstract
Background Many patients with gastric cancer present with late stage disease. Palliative gastrectomy remains a contentious intervention aiming to debulk tumour and prevent or treat complications such as gastric outlet obstruction, perforation and bleeding.

Methods We conducted a systematic review of the literature for all papers describing palliative resections for gastric cancer and reporting peri-operative or survival outcomes. Data from peri-operative and survival outcomes were meta-analysed using random effects modelling. Survival data from patients undergoing palliative resections, non-resective surgery and palliative chemotherapy were also combined. This study was registered with the PROSPERO database (CRD42019159136).

Results One hundred and twenty-eight papers which included 58,675 patients contributed data. At 1 year, there was a significantly improved survival in patients who underwent palliative gastrectomy when compared to non-resectional surgery and no treatment. At 2 years following treatment, palliative gastrectomy was associated with significantly improved survival compared to chemotherapy only; however, there was no significant improvement in survival compared to patients who underwent non-resectional surgery after 1 year. Palliative resections were associated with higher rates of overall complications versus non-resectional surgery (OR 2.14; 95% CI, 1.34, 3.46; \( p < 0.001 \)). However, palliative resections were associated with similar peri-operative mortality rates to non-resectional surgery.

Conclusion Palliative gastrectomy is associated with a small improvement in survival at 1 year when compared to non-resectional surgery and chemotherapy. However, at 2 and 3 years following treatment, survival benefits are less clear. Any survival benefits come at the expense of increased major and overall complications.

Keywords Stomach neoplasms · Gastrectomy · Survival

Introduction
Primary gastric cancer (GC) is the fifth most common malignancy worldwide and frequently presents at a late and incurable stage [1]. The majority of patients present with either stage 3 or 4 disease and many will have already developed metastasis [2, 3] with many patients surviving less than a year after initial diagnosis [4, 5]. Although the incidence of GC is declining, there are still over 5000 new diagnoses every year in the UK alone and it continues to be the 3rd biggest cause of cancer-related deaths globally [6–8].

Localised GC is often managed with combined resection and chemotherapy owing to a significant body of evidence which demonstrates its survival benefit compared to surgery alone [9–11]. However, advanced GC is generally regarded as...
incurable and resection is often not considered owing to the extent of local tumour invasion and/or the presence of distant metastases [12]. Progressive tumour growth means patients are at risk of tumour-related complications such as gastric outlet obstruction, perforation and bleeding, all of which can lead to reduced quality of life, emergency surgery and ultimately a reduction in life span.

Palliative gastrectomy (PG), comprising of either total, subtotal or distal gastrectomy, is recognised as a treatment for alleviating or preventing these complications, yet its use remains a contentious topic owing to the high-risk nature of the procedure and mixed evidence for its survival benefit in advanced GC [13–15].

Previous evidence has not only demonstrated the absence of any survival benefit from PG but has also shown no improvement in quality of life and an increased number of chemotherapy-associated adverse events [14, 15]. The REGATTA trial, the only phase III randomised control trial comparing chemotherapy alone and gastrectomy followed by chemotherapy showed no survival benefit and concluded that palliative gastrectomy in patients with metastatic gastric cancer cannot be justified [14]. Some authors have criticised the REGATTA trial for including large numbers of patients requiring total gastrectomy, using oral rather than intra-venous chemotherapy treatment regimens and grouping patients with different sites of metastatic disease together as these factors could affect the interpretation of the results [16].

There is a growing body of non-randomised evidence suggesting that PG not only provides symptomatic relief but can also extend survival [17–20]. With continued uncertainty surrounding the efficacy of PG in advanced GC, the aim of this systematic review and meta-analysis was to analyse both operative and survival outcomes following palliative gastrectomy for advanced primary gastric cancer.

**Methods**

**Search Strategy**

This study was prospectively registered with the PROSPERO database of systematic reviews (CRD42019159136). A systematic literature search was undertaken by one researcher (SK) using the PubMed, EMBASE and Cochrane Library databases on 25th January 2020. Search terms included ‘palliative gastrectomy’ or ‘palliative total gastrectomy’ or ‘palliative subtotal gastrectomy’ or ‘palliative resection’ and ‘stomach neoplasms’ or ‘gastric cancer’ or ‘gastric adenocarcinoma’ or ‘stomach cancer’. Outcomes including ‘post-operative complications’, ‘mortality’, ‘disease free survival’, ‘overall survival’ and ‘quality of life’ were included in the search. Full details of the literature search terms used can be found in Supplementary table 1. The results of the literature search were reported in accordance with the PRISMA guidelines (Fig. 1).

**Inclusion and Exclusion Criteria**

Inclusion criteria were (1) studies reporting outcomes following palliative gastrectomy for primary gastric adenocarcinoma and (2) human studies published in the English language. Exclusion criteria were (1) review articles, case reports, letters, editorials and conference abstracts; (2) studies which exclusively report outcomes for oesophagectomy, oesophagogastrectomy, surgical bypass procedures or curative gastrectomy; (3) studies in which outcomes for palliative gastrectomy were combined with the outcomes of other surgical procedures; (4) gastric cancers other than primary adenocarcinoma.

![Fig. 1 PRISMA diagram of study inclusion](image-url)
All studies generated by the literature search were screened by three independent reviewers for their relevance based on the title, abstract and study type using the above inclusion/exclusion criteria. All duplications were excluded. In the instance, there was uncertainty about the relevance of a study, the advice was sought of all authors and a final decision was made. Where studies were excluded, the reason for exclusion was verified by a fourth reviewer. For those studies which remained following this initial screening process, full texts were obtained and reviewed in detail by the same three to produce a final list of all included studies.

Study Outcomes

The primary outcome was overall survival following palliative gastrectomy for primary gastric cancer. Secondary outcomes included overall post-operative complications, major complications, anastomotic leak, pulmonary complications, mortality, overall survival rates (1-, 2-, 3- and 5-year), recurrence-free survival and self-reported quality of life measures.

Data Extraction

Data was extracted for all included studies by three independent reviewers and any queries were resolved by consensus with all authors. Data was extracted under the following headings: year of publication, study duration, study country, study design, number of study centres, use of comparison groups, overall study sample size, treatment group sample size, stage of gastric cancer, definition of palliative gastrectomy, tumour location, metastasis location, tumour histology, risk factors and chemotherapy use. In addition to extracting data for patients undergoing palliative gastrectomy, where available, data was extracted for other treatment groups under the broad headings of ‘curative gastrectomy’, ‘chemotherapy only’, ‘non-resectional surgery’ and ‘no surgery’. This data was collected to enable a comparison to the main intervention of interest, palliative gastrectomy.

Assessment of Methodological Quality

Three researchers assessed the methodological quality of all included studies using the Newcastle-Ottawa Quality Assessment Scale (NOS) for all comparative cohort studies. This score was omitted in the instance that a study was a non-comparative cohort study, for which the NOS is not valid. The overall grading of each study is given in results supplementary table 1.

Statistical Analysis

This systematic review and meta-analysis was conducted in accordance with the recommendations of the Cochrane Library and MOOSE guidelines [15]. For categorical variables, analysis was performed by calculating the odds ratio (OR). For survival analysis, relative risk (RR) statistics were calculated. Random effects modelling, using the DerSimonian-Laird method was used for the meta-analysis of outcomes. Heterogeneity between studies was assessed using the $I^2$ value in order to determine the degree of variation not attributable to chance alone. $I^2$ values were considered to represent low, moderate and high degrees of heterogeneity where values were < 25%, 25–75%, and > 75%, respectively. Assessment of small study bias was carried out by visual assessment of funnel plots and egger regressions. Statistical significance was considered when $p < 0.05$. Statistical analyses were performed using R statistical software (R version 3.5.2, R Foundation for Statistical Computing, Vienna, Austria).

Results

Study Characteristics

The literature search identified 128 studies reported according to the PRISMA guidelines as shown in Fig. 1. Studies identified were from North America ($n = 14$), South America ($n = 7$), Australasia ($n = 72$) and Europe ($n = 35$). The majority of studies were retrospective cohort studies ($n = 123$), with the remainder prospective cohort studies ($n = 3$) and RCTs ($n = 2$). Sixty-one studies identified were reported after 2010, the remaining 67 studies before 2010. Of the studies that reported on either clinical or pathological tumour stage, 41 of 91 studies consisted entirely of patients with T stage 4 disease. On average across 91 studies reporting the percentage of patients with T stage 4 disease, 68.6% of patients had T stage 4 disease. There was considerable variation in whether resections were defined as palliative due to the advanced T stage of the primary tumour or due to distant metastasis (Table 1). Across studies containing a proportion of patients with metastatic disease, 9 studies of 93 included only patients with lymph node metastases, whilst 84 included patients with a mixture of metastases sites. Of these, 41 of 84 studies included patients with liver metastases, 14 studies included patients with lung metastases and 40 included patients with peritoneal metastases.

Reporting Standards and Methodological Quality

Study quality was assessed using NOS, median 8, ranging between 5 and 9, indicating generally high quality cohort studies (Supplementary Table 1). A summary of studies reporting the impact of intervention type on morbidity and mortality is provided in Table 2.
| Study (Ref.) | Study year | Study country | Centre number | Study type | Total patients | Number TIV | Location | Mets | Histology |
|-------------|------------|---------------|---------------|------------|----------------|------------|----------|------|-----------|
| Lulu 1974 [21] | 1954–1970 | USA | Single | RCS | 100 | | Mixed | Distant | AC |
| Zacho 1974 [22] | 1949–1969 | Denmark | Single | RCS | 776 | | Mixed | Distant | AC |
| Zwaveling 1976 [23] | 1958–1972 | Netherlands | Single | RCS | 217 | | | AC |
| Nelson 1982 [24] | 1970–1975 | Australia | Single | RCS | 229 | | Mixed | | AC |
| Yap 1982 [25] | 1950–1974 | USA | Single | RCS | 465 | | | AC |
| Choi 1982 [26] | 1974–1979 | Hong Kong | Single | RCS | 119 | | Mixed | | AC |
| Meijer 1983 [27] | 1965–1981 | Netherlands | Single | RCS | 204 | | | AC |
| Yan 1985 [28] | 1958–1982 | USA | Single | RCS | 196 | | | AC |
| Cunningham 1987 [29] | 1974–1984 | UK | Single | RCS | 328 | | Mixed | | |
| Bozzetti 1987 [30] | 1965–1980 | Italy | Single | RCS | 294 | | | Distant | AC |
| de Calan 1988 [31] | 1968–1983 | France | Single | RCS | 91 | | 8 | Proximal third | AC |
| Butler 1989 [32] | 1979–1988 | USA | Single | RCS | 27 | | 14 | | AC |
| Haugstvedt 1989 [18] | 1982–1984 | Norway | Multiple | PCS | 1165 | | 460 | | AC |
| Carmalt 1990 [33] | 1974–1987 | Australia | Single | RCS | 511 | | Mixed | | AC |
| Habu 1990 [34] | 1972–1986 | USA | Single | RCS | 196 | | 126 | | Distant |
| Nakajima 1991 [35] | 1846–1988 | Tokyo | Single | RCS | 811 | | 811 | | |
| Yonemura 1991 [36] | 1978–1988 | Japan | Single | RCS | 76 | | 76 | | Lymph node |
| Monson 1991 [37] | 1980–1989 | USA | Single | RCS | 55 | | 17 | | AC |
| Maehara 1992 [1, 38] | 1965–1985 | Japan | Single | RCS | 194 | | 194 | Mixed | Distant |
| Maehara 1992 [39] | 1965–1985 | Japan | Single | RCS | 1500 | | 1116 | Mixed | Distant |
| Hugueri 1992 [40] | 1970–1988 | France | Single | RCS | 197 | | | | AC |
| Maehara 1992 [41] | 1965–1985 | Japan | Single | RCS | 1352 | | | Mixed | Distant |
| Baba 1992 [42] | 1975–1980 | Japan | Single | RCS | 119 | | 105 | Mixed | Distant |
| Geoghegan 1993 [43] | 1982–1986 | UK | Single | RCS | 114 | | | | Distant |
| Ti 1993 [44] | 1979–1992 | Singapore | Single | RCS | 160 | | 88 | | Antrum and cardia |
| Crookes 1995 [45] | 1988–1993 | USA | Single | RCS | 204 | | 120 | | Mixed |
| Chow 1995 [46] | 1985–1990 | Hong Kong | Single | RCS | 38 | | | Mixed | Distant |
| Arak 1996 [47] | 1983–1987 | Finland | Single | RCS | 203 | | | | AC |
| Saito 1996 [48] | 1964–1987 | Japan | Single | RCS | 116 | | 116 | | Distant |
| Centigoya 1998 [49] | 1982–1990 | Chile | Single | RCS | 134 | | | | Mixed |
| Kikuchi 1998 [50] | 1971–1990 | Japan | Multiple | RCS | 122 | | | | Mixed |
| Sanchez-Bueno 1998 [51] | 1979–1994 | Spain | Single | RCS | 297 | | 51 | Mixed | | AC |
| Piso 1998 [52] | 1986–1997 | Germany | Single | RCS | 64 | | 44 | Mixed | Distant |
| Ouchi 1998 [15] | 1990–1996 | Japan | Single | RCS | 95 | | 62 | | Distant |
| Piso 1998 [53] | 1986–1997 | Germany | Single | RCS | 33 | | 16 | Mixed | Distant |
| Study (Ref.) | Study year | Study country | Centre number | Study type | Total patients | Number TIV | Location | Mets | Histology |
|-------------|------------|---------------|---------------|------------|----------------|------------|----------|------|-----------|
| Lo 1999 [54] | 1988–1993  | Taiwan        | Single        | RCS        | 1642           | 747        |          |      | AC        |
| Doglietto 1999 [55] | 1981–1995  | Italy         | Single        | RCS        | 305            | 305        |          |      | AC        |
| Llanos 1999 [56] | 1975–1993  | Chile         | Single        | RCS        |                |            |          |      | AC        |
| Saidi 1999 [57] | 1988–1996  | Iran          | Single        | RCS        | 70             | 49         |          |      | Proximal half |
| Doglietto 2000 [58] | 1981–1995  | Italy         | Single        | RCS        | 639            | 305        |          |      | Mixed     |
| Ikeguchi 2001 [59] | 1985–1996  | Japan         | Single        | RCS        | 324            | 64         |          |      | Mixed     |
| Hanazaki 2001 [60] | 1988–1996  | Japan         | Single        | RCS        | 184            | 145        |          |      | Mixed     |
| Dhar 2001 [61] | 1980–1998  | Japan         | Single        | RCS        | 150            | 150        |          |      | AC, undiff |
| Fujisaki 2001 [62] | 1984–1998  | Japan         | Single        | RCS        | 43             | 43         |          |      | Distant   |
| Bonenkamp 2001 [63] | 1989–1993  | Denmark       | Single        | RCS        | 285            |            |          |      | Mixed     |
| Liu 2002 [64] | 1995–1998  | USA           | Single        | RCS        | 57             |            |          |      | Mixed     |
| Wang 2002 [65] | 1994–2000  | Taiwan        | Single        | RCS        | 415            | 415        |          |      | Mixed     |
| Collard 2003 [66] | 2003–2008  | Belgium       | Single        | RCS        | 216            | 12         |          |      | Mixed     |
| Yoshikawa 2003 [67] | 1989–2000  | Japan         | Single        | RCS        | 100            | 100        |          |      | Mixed     |
| Gill 2003 [68] | 1978–1997  | Canada        | Single        | RCS        | 2043           |            |          |      | Mixed     |
| Kobayashi 2004 [69] | 1193–2000  | Japan         | Single        | RCS        | 82             | 40         |          |      | Distant   |
| Moriwaki 2004 [70] | 1981–2004  | Japan         | Single        | RCS        | 382            | 382        |          |      | Distant   |
| Kahlke 2004 [71] | 1992–2001  | Germany       | Single        | RCS        | 169            | 169        |          |      | Mixed     |
| Medina-Franco 2004 [17] | 1995–2000  | Mexico        | Single        | RCS        | 76             |            |          |      | Mixed     |
| Zhang 2004 [72] | 1972–2000  | China         | Single        | RCS        | 2613           | 622        |          |      | Mixed     |
| Gorbunov 2005 [73] | 1990–1997  | Czech Republic| Multiple      | RCS        | 283            | 90         |          |      | Mixed     |
| Kunisaki 2005 [74] | 1980–1999  | Japan         | Single        | RCS        | 183            | 112        |          |      | Mixed     |
| Saidi 2005 [75] | 1990–2000  | USA           | Multiple      | RCS        | 105            | 105        |          |      | Mixed     |
| Alici 2006 [76] | 1999–2002  | Turkey        | Single        | RCS        | 138            | 138        |          |      | Mixed     |
| Samarasam 2006 [77] | 1999–2003  | India         | Single        | PCS        | 151            | 117        |          |      | Distant   |
| Onate-Ocana 2007 [78] | 1987–2005  | Mexico        | Single        | RCS        | 132            | 113        |          |      | Mixed     |
| Nazi 2007 [79] | 1997–2004  | Turkey        | Single        | RCS        | 74             | 74         |          |      | Mixed     |
| Lim 2007 [80] | 1989–2001  | USA           | Single        | RCS        | 63             | 63         |          |      | Mixed     |
| Lello 2007 [81] | 1984–2004  | Norway        | Single        | RCS        | 356            | 164        |          |      | Mixed     |
| Mizutani 2007 [82] | 1992–2004  | Japan         | Single        | RCS        | 26             | 26         |          |      | Distant   |
| Nazi 2007 [83] | 1997–2004  | Turkey        | Single        | RCS        | 121            | 74         |          |      | Distant   |
| Kim 2007 [84] | 1986–2000  | South Korea   | Single        | RCS        | 630            | 214        |          |      | Distant   |
| Pacelli 2008 [85] | 1981–2005  | Italy         | Single        | RCS        | 400            | 88         |          |      | Mixed     |
| Du 2008 [86] | 2005–2007  | China         | Single        | RCS        | 43             | 43         |          |      | Mixed     |
| Lin 2008 [87] | 1994–2001  | China         | Single        | RCS        | 389            | 389        |          |      | Distant   |
| Study (Ref.) | Study year | Study country | Centre number | Study type | Total patients | Number TIV | Location | Mets | Histology |
|--------------|------------|---------------|---------------|------------|----------------|------------|----------|------|-----------|
| Park 2009 [88] | 1996–2005 | Korea         | Single        | RCS        | 128            | 12         | Mixed    |      | AC        |
| Lupasacu 2010 [89] | 2003–2008 | Romania       | Single        | RCS        | 140            | 140        | Mixed    |      | AC        |
| Huang 2010 [90] | 1988–2008 | Taiwan        | Single        | RCS        | 2678           | 166        | Mixed    |      | AC        |
| Hioki 2010 [91] | 1993–2004 | Japan         | Single        | RCS        | 101            | 101        | Mixed    |      | AC, undiff |
| Sah 2010 [92] | NS         | China         | Single        | RCS        | 1639           | 398        | Mixed    |      |           |
| Ozer 2010 [93] | 2002 - 2007 | Turkey    | Single        | RCS        | 549            | 218        | Mixed    |      | AC        |
| Li 2010 [94]  | 1992–2002  | China         | Single        | RCS        | 253            | 51         | Mixed    |      | AC, undiff |
| Xue 2010 [95] | 1993–2004  | China         | Single        | RCS        | 630            | 630        | Mixed    |      | Lymph node AC |
| Turanli 2010 [96] | 2005–2008 | Turkey        | Single        | RCS        | 62             | 62         | Mixed    |      | AC        |
| Schauer 2011 [97] | 2011       | Germany       | Single        | RCS        | 120            | 38         | Mixed    |      | AC        |
| Al-Amawi 2011 [98] | 1998–2009 | Poland        | Single        | RCS        | 105            | 105        | Mixed    |      | AC        |
| Tanizawa 2011 [99] | 2002–2009 | Japan         | Single        | RCS        | 18             |            |         |      |           |
| Zhang 2011 [100] | 1991–2005  | China         | Single        | RSC        | 1171           | 529        | Proximal |      | AC, undiff |
| Izuishi 2011 [101] | 1984–2008 | Japan         | Single        | RCS        | 121            | 121        | Mixed    |      | AC        |
| Lai 2011 [102] | 1988–2009  | Taiwan        | Single        | RCS        | 295            | 195        | Mixed    |      | Lymph node AC |
| Miki 2012 [103] | 2012       | Japan         | Single        | RCS        | 50             | 40         | Mixed    |      | AC        |
| Kokkola 2012 [104] | 2000–2009 | Finland       | Single        | RCS        | 55             | 55         | Mixed    |      | AC        |
| Shim 2012 [105] | 1989–2005  | Korea         | Single        | RCS        | 278            |            | Mixed    |      | AC, undiff |
| Alonso-Larraga 2012 [106] | 2005–2010 | Mexico        | Single        | RCS        | 113            | 113        | Mixed    |      | AC        |
| Tokunaga 2012 [107] | 2002–2008 | Japan         | Single        | RCS        | 148            |            | Mixed    |      | AC        |
| Amaral 2012 [108] | 1998–2007  | Portugal      | Single        | RCS        | 155            | 59         | Mixed    |      | AC        |
| Naka 2012 [109] | 1991–2007  | Japan         | Single        | RCS        | 233            |            |         |      | AC        |
| Chang 2012 [110] | 1999–2004  | South Korea   | Single        | RCS        | 257            |            | Mixed    |      | AC        |
| Kang 2013 [111] | 2002–2010  | Taiwan        | Single        | RCS        | 172            | 172        | Mixed    |      | AC        |
| Keranen 2013 [112] | 1999–2010  | Finland       | Single        | RCS        | 97             | 6          | Mixed    |      | AC        |
| He 2013 [113] | 2008–2012  | China         | Single        | RCS        | 737            | 224        | Mixed    |      | AC        |
| Ikeguchi 2013 [114] | 2003–2010 | Japan         | Single        | RCS        | 96             | 96         |         |      | AC        |
| Xia 2014 [115] | 2014       | China         | Single        | RCS        | 119            | 115        | Mixed    |      | AC        |
| Kwon 2014 [116] | 1999–2009  | Korea         | Single        | RCS        | 769            | 228        | Mixed    |      | AC        |
| Zeeneldin 2014 [117] | 2003–2007 | Egypt         | Single        | RCS        | 168            | 58         | Mixed    |      | AC        |
| Zeng 2014 [118] | 2004–2010  | China         | Multiple      | RCS        | 533            | 41         | Mixed    |      | AC        |
| Jeong 2014 [119] | 2004–2011  | South Korea   | Single        | RCS        | 197            | 142        | Mixed    |      | AC        |
| Kim 2014 [120] | 2003–2012  | Korea         | Single        | RCS        | 43             | 8          |         |      | AC, undiff |
| Da Costa 2015 [121] | 1988–2011 | Brazil        | Single        | RCS        | 413            |            | Mixed    |      | Lymph node AC |
| Matsumoto 2015 [122] | 2002–2011 | Japan         | Single        | RCS        | 45             |            | Mixed    |      | AC        |
Table 1 (continued)

| Study (Ref.)  | Study year | Study country | Centre number | Study type | Total patients | Number TIV | Location | Mets | Histology |
|---------------|------------|---------------|---------------|------------|----------------|------------|----------|------|-----------|
| Yao 2015 [123] | 2003–2010  | China         | Single        | RCS        | 49             | 49         | Mixed    | Distant |           |
| Yang 2015 [124] | 2006–2013  | China         | Not specified | RCS        | 267            | 267        | Mixed    | Distant | AC        |
| Ebinger 2016 [19] | 1998–2009  | USA           | Multiple      | RCS        | 8249           | 8249       | Mixed    |       |           |
| Dong 2016 [125] | 2002–2012  | China         | Single        | RCS        | 47             | 47         | Mixed    |       |           |
| Coimbra 2016 [126] | 1988–2012  | Brazil        | Single        | RCS        | 179            | 179        | Mixed    | AC    |           |
| Chiu 2016 [127]  | 2008–2012  | China         | Single        | RCS        | 173            | 173        | Mixed    | AC    |           |
| Fujitani 2016 [14] | 2016       | Multiple      | Multiple      | RCT        | 89             | 89         | Mixed    | Distant | AC        |
| Musri 2016 [128] | 2002–2015  | Turkey        | Single        | RCS        | 288            | 288        | Distant  | AC    |           |
| Ikeguchi 2016 [129] | 2003–2012  | Japan         | Single        | RCS        | 78             | 78         | AC       |       |           |
| Nie 2016 [130]  | 2000–2014  | China         | Multiple      | RCS        | 371            | 371        | Mixed    | Distant | AC        |
| Al-Batran 2017 [12] | 2018       | Germany       | Multiple      | RCT        | 238            | 238        | Mixed    | Distant | AC        |
| Tokunaga 2016 [131] | 2002–2011  | Japan         | Single        | RCS        | 137            | 137        | Mixed    | AC    | undiff    |
| Fujitani 2017 [132] | NS         | Japan         | Multiple      | PCS        | 104            | 104        | Distant  | AC    |           |
| Hsu 2017 [133]   | 2000–2010  | Taiwan        | Single        | RCS        | 333            | 333        | Mixed    | Distant | AC        |
| Fornaro 2017 [134] | 2002–2015  | Italy         | Multiple      | RCS        | 513            | 513        | Mixed    | Distant | AC        |
| Yuan 2017 [135]   | 2000–2014  | China         | Multiple      | RCS        | 201            | 201        | Mixed    | Distant | AC        |
| Fukuchi 2018 [136] | 2005–2017  | Japan         | Single        | RCS        | 94             | 15         | Mixed    | Distant |           |
| Warschkow 2018 [20] | 2017       | USA           | Multiple      | RCS        | 7026           | 7026       | Mixed    | Distant | AC        |
| Picado 2018 [137] | 2004–2014  | USA           | Multiple      | RCS        | 3175           | 260        | Mixed    | Distant | AC        |
| Yuan 2018 [138]   | 2006–2014  | China         | Single        | RCS        | 384            | 384        | Mixed    | Distant | AC        |
| Yang 2019 [139]   | 2004–2013  | China         | Single        | RCS        | 80             | 80         | Mixed    | Distant | AC        |
| Omori 2019 [140]  | 2002–2014  | Japan         | Single        | RCS        | 40             | 40         | Mixed    | Distant | AC        |
| Matsubara 2019 [141] | 2004–2015  | Japan         | Single        | RCS        | 81             | 81         | Mixed    | Distant | AC        |

Ref., reference; Number TIV, number of patients with T stage 4 tumours; AC, adenocarcinoma; Location, primary tumour localisation within the stomach; RCS, retrospective cohort study; RCT, randomised controlled trial.
Peri-operative Outcomes

Overall Complications

Fifteen studies reported data on overall complications comparing patients undergoing palliative surgery compared to non-resectional procedures. Palliative gastrectomy was associated with an increase in overall complications compared to non-resectional surgery (OR 2.15; 95% CI, 1.34–3.46; p < 0.001; I² = 46%) (Table 3). Egger regression analysis suggested a significant publication bias (p = 0.004), with a Duval and tweedie imputed OR and 95% CI, 1.43 (0.81, 2.54). Seventeen studies reported data on overall complications comparing palliative surgery to curative intent surgery. Palliative surgery was associated with an increase in overall complications compared to curative surgery (OR 1.46; 95% CI, 1.18–1.79; p < 0.001; I² = 47%). No significant publication bias was identified through egger regression testing (p = 0.871).

Major Complications

Two studies reported data on major complications comparing patients undergoing palliative gastrectomy compared to non-resectional procedures. Palliative surgery was associated with an increase in major complications compared to non-resectional surgery (OR 3.41; 95% CI, 1.42, 8.20; p < 0.001; I² = 0%) (Table 3). Insufficient data were available for egger regression testing. Nine studies reported data on overall complications comparing palliative surgery to curative intent surgery. Palliative surgery was associated with an increase in major complications compared to curative surgery (OR 1.51; 95% CI, 0.87, 2.52; p = 0.12; I² = 84%). No significant publication bias was identified through egger regression testing (p = 0.702).

Anastomotic Leak

Eleven studies reported data on anastomotic leak comparing patients undergoing palliative surgery compared to non-resectional procedures. Palliative Surgery was associated with an increase in anastomotic leak compared to non-resectional surgery (OR 2.35; 95% CI, 1.14, 4.84; p = 0.02; I² = 0%) (Table 3). Egger regression analysis suggested an insignificant publication bias (p = 0.654). Thirteen studies reported data on anastomotic leak comparing palliative surgery to curative intent surgery. Palliative surgery was associated with similar rates of anastomotic leak compared to curative surgery (OR 1.01; 95% CI, 0.56, 1.42; p = 0.98; I² = 71%). No significant publication bias was identified through egger regression testing (p = 0.945).
Early Post-operative Mortality

Nineteen studies reported data on early post-operative mortality comparing patients undergoing palliative surgery compared to non-resectional procedures. Palliative surgery was not associated with a significant increase in early post-operative mortality compared to non-resectional surgery (OR 1.10; 95% CI, 0.73, 1.66; \( p = 0.66; I^2 = 21\% \)). Egger regression analysis suggested an insignificant publication bias (\( p = 0.495 \)). Twenty-nine studies reported data on early post-operative mortality comparing palliative surgery to curative intent surgery. Palliative surgery was associated with an increase in early post-operative mortality compared to curative surgery (OR 1.89; 95% CI, 1.34, 2.65; \( p = 0.98; I^2 = 43\% \)). No significant publication bias was identified through egger regression testing (\( p = 0.673 \)).

Long-term Survival

1-Year Survival

Twenty studies reported numbers surviving at 1 year following palliative surgery, non-resectional surgery, chemotherapy or no treatment. Palliative surgery was associated with an improved 1-year survival compared to non-resectional surgery (RR 0.421, 0.197–0.909; \( p = 0.044 \)), chemotherapy (RR 0.734, 0.575–0.963; \( p = 0.026 \)) and no treatment (OR 0.381, 0.176–0.827; \( p = 0.015 \)) (Table 4).

2-Year Survival

Seventeen studies reported numbers surviving at 2 years following palliative surgery, non-resectional surgery, chemotherapy or no treatment. Palliative surgery was associated with an improved 2-year survival compared to non-resectional surgery (RR 0.508, 0.347–0.742 < 0.001) and no treatment (RR 0.277, 0.239–0.326; \( p < 0.001 \)) (Table 4).

3-Year Survival

Eight studies reported numbers surviving at 3 years following palliative surgery, non-resectional surgery, chemotherapy or no treatment. Palliative surgery was associated with an improved 3-year survival compared to chemotherapy (RR

### Table 3 Relative risk and 95% confidence intervals of different treatment strategies versus palliative gastrectomy at 1-, 2-, 3- and 5-year survival

|                | \( N \) | \( RR \)  | 95% CI       | \( p \)  | \( I^2 \) |
|----------------|------|-------|--------------|------|-------|
| **1-year survival** |      |       |              |      |       |
| Palliative gastrectomy vs. chemotherapy only | 5    | 0.734 | 0.559–0.963  | 0.0256 | 81%   |
| Palliative gastrectomy vs. non-resectional procedures | 7    | 0.421 | 0.197–0.909  | 0.0435 | 82%   |
| Palliative gastrectomy vs. no intervention | 8    | 0.381 | 0.176–0.827  | 0.0147 | 91%   |
| **2-year survival** |      |       |              |      |       |
| Palliative gastrectomy vs. chemotherapy only | 6    | 0.508 | 0.352–0.744  | 0.040 | 81%   |
| Palliative gastrectomy vs. non-resectional procedures | 5    | 0.432 | 0.150–1.194  | 0.4434 | 85%   |
| Palliative gastrectomy vs. no intervention | 6    | 0.277 | 0.239–0.326  | < 0.001 | 0%   |
| **3-year survival** |      |       |              |      |       |
| Palliative gastrectomy vs. chemotherapy only | 4    | 0.578 | 0.298–1.07   | 0.2285 | 70%   |
| Palliative gastrectomy vs. non-resectional procedures | 1    | -    | -            | -    | -    |
| Palliative gastrectomy vs. no intervention | 3    | 0.225 | 0.181–0.284  | < 0.001 | 0%   |
| Papers published post-2010 subgroup |      |       |              |      |       |
| **1-year survival** |      |       |              |      |       |
| Palliative gastrectomy vs. chemotherapy only | 5    | 0.734 | 0.559–0.963  | 0.0256 | 81%   |
| Palliative gastrectomy vs. non-resectional procedures | 1    | -    | -            | -    | -    |
| Palliative gastrectomy vs. no intervention | 1    | -    | -            | -    | -    |
| **2-year survival** |      |       |              |      |       |
| Palliative gastrectomy vs. chemotherapy only | 6    | 0.508 | 0.347–0.742  | < 0.001 | 81%   |
| Palliative gastrectomy vs. non-resectional procedures | 1    | -    | -            | -    | -    |
| Palliative gastrectomy vs. no intervention | 2    | 1.101 | 0.407–2.974  | 0.562 | 0%    |
| **3-year survival** |      |       |              |      |       |
| Palliative gastrectomy vs. chemotherapy only | 5    | 0.567 | 0.299–1.074  | 0.0816 | 54%   |
| Palliative gastrectomy vs. non-resectional procedures | 1    | -    | -            | -    | -    |
| Palliative gastrectomy vs. no intervention | 1    | -    | -            | -    | -    |
Discussion

This review identifies an association between palliative gastrectomy and improved overall survival for patients with gastric cancer treated palliatively, compared to chemotherapy, non-resectional surgery and no treatment, at 1 year. After 1 year, palliative gastrectomy was not associated with a survival benefit over non-resectional surgery. Significantly, palliative gastrectomy was associated with increased morbidity compared to non-resectional surgery; however, this was not simultaneously associated with increased peri-operative mortality.

This study encompasses all relevant trials up until January 2020. Surgical techniques and oncological therapies have improved markedly during the inclusion period which extends from 1974 to 2018. Potential improvements in clinical practice may have enabled improved patient selection for gastrectomy. Improvement in surgical and oncological techniques concurrently with improved patient selection aims to optimise survival for those fit for some form of resection. Current patient selection uses criteria such as patient performance status, co-morbidity, extent of disease and importantly patient choice. The extent to which biology of the disease dictates outcome is poorly understood, however, with ongoing research into the genetics of gastric cancer [142, 143] with the potential to further refine selection in the future, further optimising outcomes [144, 145].

The study, although comprehensive, including 128 papers which included 58,675 patients did include studies from over 40 years, some of which may have limited clinical relevance; however, subgroup analyses of papers published in the last decade did not show significantly different results. The study did not incorporate outcomes for palliative gastrectomy which were combined with the outcomes of other surgical procedures such as cytoreductive surgery (CRS) which together may improve survival for those who would otherwise receive palliative oncological therapies. The precise reason for palliative surgery and the extent of disease burden was heterogeneous throughout the studies identified and the lack of current clinical guidelines or consensus on this topic makes this extremely difficult to standardise. Very few studies reported on health-related quality of life measures, following palliative gastrectomy. In an era where health research aims to re-

### Table 4

| 1-year survival | 2-year survival | 3-year survival |
|-----------------|-----------------|-----------------|
| Palliative gastrectomy vs. chemotherapy only | Palliative gastrectomy vs. chemotherapy only | Palliative gastrectomy vs. chemotherapy only |
| Palliative gastrectomy vs. non-resectional procedures | Palliative gastrectomy vs. non-resectional procedures | Palliative gastrectomy vs. non-resectional procedures |
| Palliative gastrectomy vs. no intervention | Palliative gastrectomy vs. no intervention | Palliative gastrectomy vs. no intervention |
| N | RR | 95% CI | p | I² |
|---|---|---|---|---|
| 5 | 0.734 | 0.559–0.963 | 0.0256 | 81% |
| 7 | 0.421 | 0.197–0.909 | 0.0435 | 82% |
| 8 | 0.381 | 0.176–0.827 | 0.0147 | 91% |
| 6 | 0.508 | 0.252–0.997 | 0.045 | 81% |
| 5 | 0.442 | 0.071–2.697 | 0.4434 | 85% |
| 6 | 0.277 | 0.239–0.326 | <0.001 | 0% |
| 4 | 0.578 | 0.298–1.12 | 0.2285 | 70% |
| 1 | - | - | - | - |
| 3 | 0.225 | 0.181–0.284 | <0.001 | 0% |

0.578, 0.298–1.12; p = 0.23) and no treatment (RR 0.225, 0.181–0.284; p < 0.001) (Table 4).
focus on patient perceived benefits, any measured improvement in health-related quality of life could be considered more important than small improvements in quantity of life with co-morbid surgical procedures.

Challenges remain as how to determine treatment choice based on the extent of local disease and whether patients with T4b disease should receive surgery. There is significant variation in unit practice as to whether patients receive a multivisceral resection (MVR) or palliative surgery. MVR is associated with a significant morbidity and mortality in excess of the accepted risks of gastrectomy [146]. This is particularly evident when distal pancreatectomy is required to achieve an R0 resection [147]. Despite this, performing an MVR to achieve an R0 resection does provide a survival advantage and should be a potential treatment option in patients deemed sufficiently fit for surgery of this magnitude [148].

The role of surgery in metastatic gastric cancer continues to evolve as treatment options mirror advances in other malignancies. Hepatectomy for colorectal liver metastasis has been shown to improve survival compared to other palliative treatment options [149]. There is now evidence to demonstrate that hepatectomy for gastric cancer metastases is associated with longer median overall survival than palliative treatments for selected patients [150, 151]. Peritoneal carcinomatosis is predominantly treated with systemic chemotherapy; however, cytoreductive surgery and heated intraperitoneal chemotherapy (CRS and HIPEC) have been shown in highly selected patients to provide a survival advantage [152, 153]. Pressurised intraperitoneal aerosol chemotherapy has also been demonstrated to be safe and provides beneficial anti-tumour activity in patients with gastric cancer peritoneal carcinomatosis [154]. Although this systematic review and meta-analysis does not specifically examine the potential beneficial adjuncts to gastrectomy, it is important to identify that achieving a survival advantage with surgery may require a multi-modal approach.

It is currently not clear to what extent oncological therapies could be used in concordance with surgery and whether patients undergoing palliative resection should be offered neo-adjuvant and adjuvant chemotherapy, as standard, particularly in an era where FLOT (5-fluorouracil, folinic acid, oxaliplatin, docetaxel) is becoming the gold standard of oncological treatment for patients with oesophago-gastric cancer. The REGATTA trial randomised patients to gastrectomy with D1 lymphadenectomy without any resection of metastatic lesions and adjuvant chemotherapy or chemotherapy alone and found no significant difference in overall survival [14]. Subsequently, there has been a trend away from the use of surgery in improving survival in patients who are known to have metastatic gastric cancer [155].

The AIO-FLOT 3 trial compared patients with limited metastatic disease who benefited from neoadjuvant FLOT to patients with resectable disease and to patients with extensive metastatic disease [12]. The trial identified that patients with limited metastatic disease who received neoadjuvant chemotherapy and proceeded to surgery showed a favourable survival when compared to expected survival for patients with metastatic disease. The trial did not determine the additional benefit of surgery in patients with limited metastatic disease who showed a good response to chemotherapy. Improvements in chemotherapy in conjunction with improving surgical techniques inclusive of a D2 gastrectomy and metastatectomy may provide improved survival for patients who previously may have been palliated.

Oncological therapies continue to develop and immunotherapy is increasingly playing a role in gastric cancer as is evident with HER2 positive tumours and the use of trastuzumab [156]. Further studies continue into the importance of HER-2 blockade in the form of trastuzumab and pertuzumab in conjunction with FLOT in the Petrarca Trial which is yet to report [157]. Increasingly immunotherapy trials continue to examine the benefits of PD1/PD-L1 and CTLA4 blockade and will likely be incorporated into the treatment pathways of advanced gastric cancer [158–160].

Conclusions

Palliative gastrectomy is associated with significant morbidity over and above non-resectional palliative surgery and gastrectomy for curative intent. Palliative gastrectomy may offer an early survival advantage compared to oncological therapies given in isolation; however, this does not extend beyond a couple of years and may well result from patient selection biases. Further research into the biology of gastric cancer and improved techniques for patient selection are required to improve overall survival for patients with palliative gastric cancer.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

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