

Evidence tabel – Lokaal palliatieve behandelingen

Auteurs, jaartal	Mate van bewijs	Studie type Follow-up	Populatie (incl. steekproef-grootte)	Patienten kenmerken	Interventie	Controle	Resultaten	Conclusie	Opmerkingen, commentaar
Hartgrink, 2002  The Netherlands	B	Prospective cohort  Follow-up not reported	285 pts with incurable gastric cancer (detected after a laparotomy as part of the Dutch Gastric Cancer Trial).  Pts had palliative treatment considered appropriate by the surgeon	Median age 65 yrs (30-86)	Palliative resection (n= 156)	Gastroenterostomy or exploratory laparotomy (n=129)	<p><i>Results: resection vs no resection</i>                      Median survival: 8.1 vs 5.4 months (p&lt;0.001)                      Mean survival: 14.3 vs 8.0 months (no p given)                      Morbidity: 38% vs 12% (p&lt;0.001)                      Median (range) hospital stay: 15 (7-154) vs 10 (3-93) days (p&lt;0.001)                      Mortality: 19 vs 13% (n.s.)</p> <p>Patients over 70 years of age had a significantly higher morbidity (p&lt;0.05) and longer hospital stay (p&lt;0.01) compared with those aged 70 years or less. The mortality rate for patients over 70 years who had resection was also higher than that of the younger patients who had resection (20 versus 9 %, p=0.06). If, however, the patient survived palliative resection, the median survival for the two age groups was nearly equal.</p> <p>For patients with one metastatic site a resection was beneficial (survival 10.5 versus 6.7 months; p=0.034). For patients with two or more metastatic sites resection had no survival advantage (5.7 versus 4.6 months; p=0.084).</p>	This study shows that patients under 70 years of age with one metastatic site will benefit from a palliative resection. For all other patients there was no survival benefit. If morbidity, hospital stay and mortality are also considered, there is probably no gain for patients aged more than 70 years undergoing palliative resection.	Bonenkamp 2001 reported on same sample of patients  Not randomized; FU not clear, no control for confounding: more severe pts were more likely to have no resection

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<p>Bonenkamp, 2001 The Netherlands</p>	<p>B</p>	<p>Prospective cohort study</p>	<p>285 gastric cancer pts who had laparotomy in a national randomized trial of lymphadenectomy and were found noncurable because of remnant tumour, peritoneal, distant lymph node or liver metastasis.</p>	<p>Median age (range) GR: 66 (33-86), 64% males  NR: 66 (30-83), 69% males</p>	<p>Gastric resection (GR n=152, of which partial n=89 or total n=63)</p>	<p>No gastric resection (NR n=133, of which bypass surgery n=55 or exploration n=78)</p>	<p>Number of signs of noncurability (tumor load) was related to the type of surgical palliation chosen by the surgeon; 1 sign -&gt; 68% palliative stomach resection &gt;1 sign -&gt; 36% palliative stomach resection  <i>Hospital mortality</i> GR: 9% (exploration: 5%; bypass: 14%) NR: 10% (partial: 10%, total: 11%)  The survival advantage of resection disappeared in the group with 2 of more positive signs</p>	<p>Palliative resection can be beneficial, especially for those patients with limited tumor load, restricted to one metastatic site. With high tumor load (i.e. 2 or more metastatic sites), survival is not influenced by surgical treatment.</p>	<p>Hartgrink 2002 reported on same sample of patients. Although there are some minor differences in the sample only additional results are presented here.</p>
<p>Medina-Franco, 2004 Mexico</p>	<p>B</p>	<p>Prospective cohort  Median 9 months</p>	<p>76 patients with gastric cancer stage IV who underwent surgery (excl criteria for surgery were visceral metastases, poor performance status or severe comorbidities)</p>	<p>Mean age 56 ± 14 yrs; 48.7% males  All patients had gastric adenocarcinoma stage IV</p>	<p>3 groups: 1) resection (n=40); total gastrectomy (n=24) and partial gastrectomy (n=16) 2) gastric bypass: gastrojejunostomy (n=10) 3) celiotomy and biopsy (n=16), jejunostomy placement (n=9) or gastrostomy placement (n=1)  (chosen by surgeons)</p>	<p>Operative complications: n=20 (26%) Surgical mortality (30-d mortality) n=2 (2.6%)  Overall survival was 8 months (4-12), and there was a difference in survival between patients who underwent resection (median survival 13 months) compared with those who underwent bypass (median survival 5 months), celiotomy, or tube placement (median survival 3 months) (p=0.001).  35 pts had a bleeding; 29 received resection and of these 83% had good palliation. 17 pts had dysphagia; 10 received resection and of these 80% had good palliation. 34 had outlet obstruction; 13 had resection and 10 had a by-pass; 85% and 60% respectively had good palliation.</p>	<p>Surgical resection for stage IV gastric carcinoma can be done with low surgical mortality and low morbidity rates. Resective procedures may confer some survival advantage in this group of patients with good palliation of symptoms compared with results obtained from bypass procedures or systemic chemotherapy. Advanced patient age, itself, should not be considered a contraindication for surgery.</p>	<p>Not randomized; small sample size; most patients in the resection group received treatment compared with those who did not</p>	

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<p>Ouchi, 1998  Japan</p>	<p>B</p>	<p>Prospective cohort</p>	<p>95 pts with gastric cancer who received palliative operations</p>	<p>Mean age; % male; tumor stage  1) 64.3 (37-85); 69%; IIIB (n=2) or IV (n=62)  2) 64.6 (41-86); 93%; IV  3) 59.8 (19-75); 63%; IV  Total: 72% male</p>	<p>3 groups:  1) palliative gastrectomy (n=64)  2) gastrojejunosteomy (n=15)  3) exploratory laparotomy (n=16)</p>		<p>Hospital death 1) 1.6% 2) 33.3% 3) 31.3% Multivariate analysis showed that type of operation was the only independent prognostic factor for survival (p=0.001).  1-year survival rate 1) 48.2% 2) 20.4% 3) 37.5% Survival was significant better for patients who underwent palliative gastrectomy compared to those who underwent gastrojejunostomy (p&lt;0.01).  QOL: Hospital-free survival (HFS) for 3 months or longer achieved in 1) 82.8% 2) 33.3% 3) 56.2% An achievement of HFS for a period of 3 months or longer in patients who underwent palliative gastrectomy was higher than that in patients who underwent gastrojejunostomy or laparotomy (p&lt;0.001 or p&lt;0.05).</p>	<p>As a palliative measure, gastrojejunostomy and total gastrectomy performed with P<sub>2</sub> or P<sub>3</sub> peritoneal dissemination had no beneficial effect on the prolongation of survival or improvement of QOL of patients with gastric cancer. The results demonstrated that depth of invasion, hepatic metastasis, and lymph node metastasis were not independent prognostic factors related to survival.</p>	<p>Not randomized; small sample size</p>
<p>Hanazaki, 1999  Japan</p>	<p>B</p>	<p>Retrospective cohort</p>	<p>83 pts who underwent palliative partial or total gastrectomy for noncurable gastric cancer</p>	<p>Group, Mean age (SD)  A: 69.0 (8.9), 65.9% males, 25% total gastrectomy, 52.3% post-operative chemo  B: 67.7 (9.0), 59.0% males, 38.5% total gastrectomy, 64.1% postoperative chemo</p>	<p>A: Gastrectomy with limited or simple lymph node dissection (D0 and D1) (n=44)</p>	<p>B: Gastrectomy with extended lymph node dissection (D2) (n=39)</p>	<p><i>Survival rates A vs. B:</i> 1-year: 49.0% vs. 82.1% (p&lt;0.01) 3-year: 39.7 vs. 25.7 (ns) 5-year: 39.7% vs. 20.5% (ns)  Median survival time after surgery, with and without distant metastasis was larger in group B (21.5 SD 6.5 vs. 16.4 SD 23.6, ns)</p>	<p>Gastrectomy with extended lymph node dissection did not contribute to improve long-term survival in patients with non-curable advanced gastric cancer. Utility of extended lymph node dissection may be relevant to improve loco-regional control, at least in prognosis &lt;1 year after surgery. Aggressive chemo may be needed to improve long-term survival for such patients.</p>	<p>Not randomized; small sample size</p>

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<p>Hanazaki, 2001 Japan</p>	<p>B</p>	<p>Retrospective cohort</p>	<p>184 pts who underwent palliative gastrectomy (PG; n=84) or unresectable operation (UO, n=100)</p>	<p>PG: Mean age 69 yrs (SD 9), 65.5% males, 52.4% peritoneal dissemination, 59.4% postoperative chemo</p> <p>UO: Mean age 65 yrs (11), 66.0% males, 53.0% peritoneal dissemination, 37.0% postoperative chemo</p>	<p>Palliative gastrectomy (PG)</p> <p>(total gastr. 28 pts; partial gastr. 56 pts)</p>	<p>Unresectable operation (UO)</p> <p>(laparotomy 51 pts, GJJ 36 pts, ileal tube insertion 13 pts)</p>	<p><i>Overall PG vs. UO</i> Median survival: 20.6 vs. 5.7 months (sign, but no p-value given) Survival rates: 6 months: 83.6% vs. 38.3% (p&lt;0.01) 1 year: 63.0% vs. 9.3% (p&lt;0.01) 2 years: 35.2% vs. 0% (p&lt;0.01)</p> <p><i>In stage IVb patients (n=103) PG vs. UO</i> 10.2 vs. 5.0 months (sign, but no p-value given) Survival rates: 6 months: 66.7% vs. 30.1% (p&lt;0.01) 1 year: 45.8% vs. 6.8% (p&lt;0.01) 2 years: 29.2% vs. 0% (p&lt;0.01)</p> <p><i>Inpatients with liver metastasis (n= 37) PG vs UO</i> 8.4 vs. 4.6 months (ns)</p>	<p>Palliative gastrectomy compared to unresectable operation may be effective for improvement of prognosis, even if stage IVb patients with peritoneal dissemination and/or distant lymph node metastasis. However, it may be unfavorable on survival of patients with synchronous liver metastasis.</p>	<p>Not randomized; groups not comparable - UO group had worse health status</p>
<p>Kunisaki, 2003 Japan</p>	<p>B</p>	<p>Retrospective cohort</p> <p>Median follow-up: 7.8 (SD 11.1) months</p>	<p>228 pts with noncurable gastric cancer with mainly peritoneal metastasis</p>	<p>Mean age (SD)</p> <p>Gastr. 61.3 (12.7), 65% males</p> <p>Non-gastr. 58.6 (11.2), 68% males</p> <p>57 pts received post-operative chemotherapy</p>	<p>Palliative gastrectomy (n=141)</p> <p>(total gastr. 74 pts; partial gastr. 67 pts)</p>	<p>No gastrectomy (n=87)</p> <p>(bypass procedure 41 pts, exploratory laparotomy 34 pts, no operation 12 pts)</p>	<p><i>Overall:</i> Sign difference in survival and between pall gastr. (median 9 months) and non-gastr (med 3 months)(no p-value given) Hospital mortality : 11.3% vs. 34.5% Postoperative morbidity: 37.5%</p> <p>Multivariate prognostic factor for survival: degree of peritoneal metastasis; sign. diff in survival between P0CY1/P1 and P2/P3 (HR 1.91; 95% CI 1.31, 2.78).</p> <p><i>Within pall. resection group:</i> Prognostic factor for survival: degree of peritoneal metastasis. Sign. diff in survival between P0CY1/P1 and P2/P3 (HR 1.25; 95%CI 1.02, 1.55).</p> <p><i>In P0VY1/P1 cases:</i> Prognostic factors for survival Resection (HR (95%CI) no vs yes: 5.86 (2.64, 13.04) Tumor diameter&lt;100mm (HR (95%CI) no vs yes: 1.78 (1.01, 3.11).</p>	<p>Palliative gastrectomy is indicated in P0CY1 or P1 cases with tumor diameters&lt;100mm. In such gastrectomy, lymph node dissection is limited to a little more than D1, which eradicates only microscopically identifiable metastatic lymph nodes near the stomach.</p>	<p>Not randomized</p>

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<p>Doglietto, 1999  Italy</p>	<p>B</p>	<p>Retrospective cohort  83.2% had follow-up &gt; 5 yrs</p>	<p>305 gastric cancer pts who did not undergo surgical treatment or who underwent palliative surgery and treated by the same surgical team</p>	<p>Mean age 63.7 yrs (SD11.6), 70.8% males</p>	<p>4 treatment groups: 1) Gastric resection (GR, n=93; 38 total, 55 distal) 2) Bypass procedure (BPP, n=78) 3) Explorative laparotomy (EL, n=72) 4) No operation (NO, n=62)</p>	<p><i>Hospital morbidity</i> Overall: 20.6%: 1) 28.0% 2) 25.6% 3) 16.6% 4) 8.0% (no p-values given)</p> <p><i>Hospital mortality</i> Overall: 9.5% 1) 11.8% (13.1% total; 10.9% distal) 2) 10.2% 3) 8.3% 4) 6.4% (no p-values given)</p> <p><i>5 year survival (p&lt;0.0001; p-value based on survival curve)</i> 1) 18.4% 2) 2.4% 3) 0.0% 4) 0.0%</p> <p><i>Median survival:</i> 1) 16.3 months 2) 7.1 months 3) 4.4 months 4) 3.1 months</p> <p><i>Multivariate prognostic variables</i> Resectional surgery (group 1, p&lt;0.0001) and tumor spread limited to local sites (p=0.008) were associated with better survival.</p> <p>Type of operation: EL vs GR: RR of death 1.96, p=0.001 BPP vs. GR: RR of death 2.34, p&lt;0.0001 NO vs. GR: RR of death 2.28, p&lt;0.0001</p> <p>Extent of spread: Distant vs. local: RR of death 1.45, p=0.039</p>	<p>The study indicated that even though there are host-related factors that govern survival in far-advanced gastric cancer, type of surgery can have significant effect on prognosis. Resectional surgery should be undertaken whenever possible in such patients, because both short-term and long-term survival advantages have been shown.</p>	<p>Not randomized; groups not comparable</p>
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Stent compared with GJJ										
Jeurnink, 2007	B	Systematic review  Search period 1996- 2006	44 Studies on Gastrojejunostomy (total of 297 patients) and stents (1046 patients) reporting results on medical effects and costs inpatients with malignant gastric outlet obstruction	2 RCTs comparing stent placement with GJJ RCT1: 15% gastric cancer RCT2: malignancy of pyloric antrum	Stent	GJJ	% based on all studies, OR's (95% CI) based on RCTs and comparative studies:  No differences between stent or GJJ found in: Technical success (96% vs 100%; OR 0.22; 0.02, 2.1 ), Early major complications (7% vs. 6%; OR 0.49; 0.1, 2.6) Late major complications (18% vs. 17%; OR 0.74; 0.1, 4.0) Persisting symptoms (8% vs. 9%).	Stent placement may be associated with favorable results in patients with a relatively short life expectancy, while GJJ is preferable in patients with more prolonged prognosis.	Applying Delphi criteria made clear that quality of the randomized trials and comparative studies was limited.  Mixed patient population	
				6 comparative studies on stent placement vs. GJJ, partly gastric cancer	Stent	GJJ				Initial clinical success was higher after stent placement (89% vs. 72%; OR 3.39; 0.8, 14.3)
				36 case series evaluating either stent placement or GJJ, partly gastric cancer	Stent or GJJ	No control group				Minor complications were less frequently seen after stent placement in the case series, but pooled analysis of randomized and comparative studies showed no difference (OR 0.75; 0.1, 5.0). Recurrent obstructive symptoms were more common after stent placement (18% vs. 1%)  Hospital stay: prolonged after GJJ compared to stent (13 days vs. 7 days) Mean survival: stent placement 105 days; GJJ 164 days.
Hosono 2007	B	Meta-analysis  Search period 1990-2006	Studies that compared endoscopic stenting (ES) and surgical gastroenterostomy (GE) for palliation of gastroduodenal obstruction due to inoperable malignant disease. One RCT and 8 comparative studies were found	1 study was on gastric cancer, other studies had 15-50% gastric cancer pts	Endoscopic stenting (ES)	Surgical gastroenterostomy (GE)	ES was found to be associated with higher clinical success (OR 2.97; 95% CI 1.34, 6.57), a shorter time from the procedure to starting oral intake (WMD -5.44 days 95% CI -7.51, -3.37), less morbidity (OR 0.40 95% CI 0.18, 0.89), lower incidence of delayed gastric emptying (OR 0.08; 95% CI 0.02, 0.41) and a shorter hospital stay (WMD -9.65 days 95% CI -11.63, -7.67) than surgical GE. There was no difference with respect to 30-day mortality (OR 0.63; 95% CI 0.23, 1.77).	ES may be a feasible alternative to surgery for the palliation of inoperable malignant gastroduodenal obstruction, with a high clinical success and low morbidity.	Quality of studies not assessed  Mixed patient population	

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Dormann, 2004	C	Systematic review  Search period 1992- 2002	Studies on safety and clinical effectiveness of self-expanding metal stents	32 cases series, of which 10 were prospective  606 patients; 32% gastric cancer patients	Stent placement	<p><i>Pooled results:</i>                      Technical success: 97%                      Clinical success following technical success: 89%                      Time to final resolution of symptoms: 3.7 days                      Mean survival: 12.1 weeks</p> <p>Procedural mortality: 0%                      Severe complications: Perforating 0.7%, bleeding 0.5%                      Non-severe complications: 26.7% (most frequent complication: stent obstruction in 17.2%)</p>	Gastroduodenal stenting offers a good palliation and is a safe and effective treatment option in patients with short remaining lifespan/ Patient selection is an issue requiring thorough consideration. Studies comparing method with surgery are needed	No control group; mixed patient population
Open versus laparoscopic GJJ (study also included in systematic reviews above)								
Mittal, 2004	B	Retrospective cohort study	46 pts who underwent surgery for malignant pyloroduodenal obstruction	Mean age (range) 1) 67.5 (44-83); 63% males 2) 68.0 (60-90); 29% males 3) 63.5 (39-82); 63% males	3 groups: 1) GJJ open (n=16) 2) GJJ laparoscopic (n=14) 3) stent (n=16)	<p>Times takes to tolerate free oral fluids                      1) med 6 days (range 3-28)                      2) med 4 (3-6)                      3) med 0 (0-1) (p&lt;0.001)</p> <p>Length of stay after procedure                      1) med 10 days (range 8-39)                      2) med 7 (5-25)                      3) med 2 (1-18) (p&lt;0.01)</p> <p>Pts who underwent surgical palliation had more complications than pts who underwent stenting (n=5 for open GJJ, 6 for laparoscopic GJJ versus 0, p=0.016).</p>	This matched study showed significant advantages for ES compared with open GJJ and laparoscopic GJJ.	Not randomized; small sample size; mixed patient population