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Surgical Palliative Bypass Versus Endoscopic Stenting For Advanced Pancreatic Head Adenocarcinoma In Gastroentrology And Hepatology Teaching Hospital

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ABSTRACT

Background: The high percentage of patients with pancreatic cancer are non-resectable and presented as jaundice at presentation. Methods of palliation in such patients with locally advanced disease comprised of endoscopic biliary endoprosthesis or surgical bypass.
Methods: This double control comperative study,that compare morbidity, mortality, hospital stay, readmission rate and survival in consecutive patients with incurable locally advanced pancreatic head adenocarcinoma. **Results:** We identified a total of 60 patients, of whom 30 underwent endoscopic stenting and 30 underwent a surgical bypass consisting of a choledochojejunostomy- Roux-en-Y and a gastrojejunostomy. There were no significant differences in complication or mortality rates between patients undergoing palliative stenting and those undergoing palliative surgery. However, after excluding admissions for chemotherapy related problems, the number of readmissions expressed as a percentage of the group population size was greater in stented patients compared with biliary bypass patients (43.3% vs. 10%, respectively;P <0.05). Overall survival amongst patients undergoing palliative bypass was significantly greater than in stented patients (382 days vs. 135 days, respectively; P <0.05).**Conclusions**: On analysis of these data, we conclude that surgical bypass represents an effective method of palliation for patients with locally advanced pancreatic head cancer. Patients need to be carefully selected with regard to both operative risk and perceived overall survival.
Keywords:pancreatic cancer, survival, surgical bypass, biliary bypass, biliary stent.

Introduction:

Pancreatic adenocarcinoma is the fourth leading cause of cancer-related mortality in the U.S. and seventh most common in Europe, due to vascular invasion or metastasis at the time of diagnosis[1,2,3],The median survival is less than six months and only a minority (10–20%) of patients are considered candidates for resection at time of diagnosis. Accurate staging requires a multidisciplinary approach including imaging, tumor markers, and if available pathology via surgical exploration, to further classify the cancer's prognosis. Laparoscopic staging to determine resectability and thus prevent unnecessary exploratory laparotomies has had low detection rates and has fallen out of favor[4]. Even with those that are selected for surgical resection, the five year survival continues to be at 15–20%, primarily due to recurrence.[5]Unfortunately, most patients are elderly and/or have an advanced stage of disease at the time of diagnosis, and are unsuitable for curative resection. Palliative treatment is usually performed to relieve thejaundice. Biliary-enteric surgical bypass has been the treatment of choice for palliation of obstructive jaundice for many years.

The introduction of a minimally invasive endoscopic stenting technique has provided a new option for clinicians, and this has become very popular procedure in the management of obstructive jaundice, The choice between surgery and endoscopic drainage is a matter of personal preference and availability of alternative techniques, Comparative studies from Western countries have shown a similar efficacy between endoscopic drainage and surgical treatment. However, there are no data to support these findings in developing countries.[6]

Up to 80% of ductal adenocarcinomas of the head of the pancreas are not resectable at presentation.[7,8]As 70–90% of patients with carcinomas of the head of the pancreas and ampullary region have jaundice at presentation, other presentation include cholangitis, pruritis, nutritional deficiencies through malabsorption, weight loss, and progressive hepatic failure[9–11], .palliation that ensures biliary drainage represents a large proportion of the hepatobiliary surgeon's workload.

Various therapeutic options have been described. Some centres advocate palliative resection ,

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arguing that it may offer a survival advantage or better palliation and has equivalent morbidity and mortality rates to bypass surgery.[12–14] but these results are disputed by other groups.[15] Other options include surgical biliary bypass incorporating either an hepatojejunostomy-(choledochojejunostomy),[16-18] cholecystojejunostomy[18,19] or choledochoduodenostomy[16,18] with or without a concomitant gastrojejunostomy.[20] More recently, these procedures have been undertaken laparoscopically, with reportedly low morbidity and mortality.[21,22] In addition, biliary endoprostheses can be employed to relieve biliary stasis. Internal drainage of the biliary tree via the transhepatic route was first described in 1978.[23,24] The introduction of endoscopically placed stents enabled the use of larger-calibre endoprostheses.[25,26] The advantage of biliary stents is that their positioning is a minimally invasive procedure which is well tolerated by patients. However, their palliative potential is limited by the recurrence of jaundice secondary to stent migration or . Tumour progression and duodenal invasion may render repeated stenting impossible..

Historically, palliative care has been seen as necessary pain and symptom control at the very end of life when 'proper measures' are futile and there is nothing more to be done.

Palliative care actually begins at the time the decision is made that the appropriate treatment is not curative. In short,the clinicians who are managing patients with pancreatic cancer are effectively practising palliative care all the time and only a few surgeons are practising potentially curative treatment. palliative approach is an attitude and quality of practice that manages incurably ill patients sensitively and effectively throughout the illness. As the end point of treatment is not cure but relief of symptoms, a different set of criteria must be used to judge the effectiveness of the management of the patient.

Objectives in palliative care are:

-relieve suffering in whatever form it takes

-optimise the quality of life

-use the patients time for maximum benifit

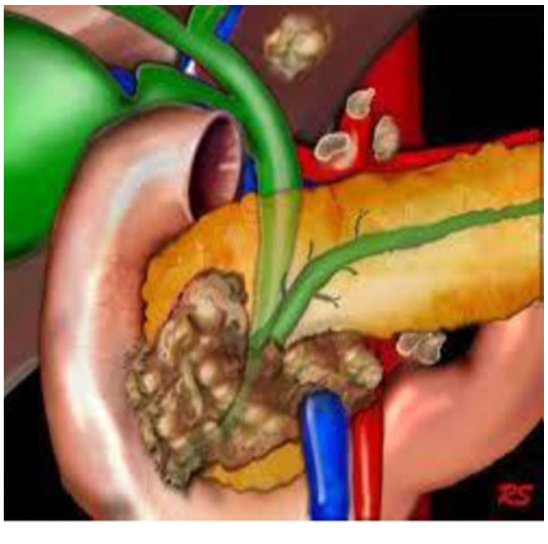
-To help the patient find ameaning in completing their life

-Ensure the end of life is natural and comfortable

Whatever is necessary to achieve a realistic outcome is alegitimate palliative measure. Thus, there is no conflict between measures which will possibly cure or only palliate -provided that such strategies are centred on the needs and wishes of the patient and family, that there is clear and good reason, that there is a clearly defined goal, and that the clinical situation is reviewed once the defined objective has been met.[27]

Palliation for patients with pancreatic cancer demands adifferent attitude to outcome by the clinician. The emphasis has been on technique, be it radical surgery, palliative surgery, endoprosthesis or nerve blockade, and the end points have been survival, hospital stay, readmission rates and relief of symptoms. However, there has been a lack of assessment of the quality of life achieved by these manoeuvres, and little documentation of how long the patient lived a symptom-free fully active normal life. For example,the patient who undergoes resection of a pancreatic cancer has a median survival of 12-15 months, yet at three months has a better performance index than the patient who was inoperable and had a lesser procedure. The palliative gain despite the poor prognosis appears worth while, but we do not know the limits to which this policy of an aggressive operative approach may be pushed in order still to maintain gain.[28]

Figure 1 : Demonstration pancreatic head adenocarcinoma.



The aim of this study was to compare morbidity and mortality rates and effectiveness of palliation between patients matched for tumour size and clinical stage who underwent palliative surgical bypass or endoscopic palliative stenting for only locally advanced pancreatic adenocarcinoma.

Patients and Methods:

Study methodology:

Cases were analysed by douple blind placebo control study for all patients who presented consecutively to GIT Hospital of from January 2015 toAugust 2016 with primary head pancreatic cancer, requiring palliative treatment for their malignant obstructive jaundice,of both gender and age between 58-72 year.

Patients were divided into two treatment groups consisting of, respectively, patients who underwent stenting +/- chemotherapy and patients who underwent palliative surgery +/- chemotherapy.

All patients with metastatic disease and ascitis proven by imaging or surgical assessment were excluded from this study. Patients with histopathological diagnoses other than adenocarcinoma were also excluded.(exclusion criteria).

Date of diagnosis was the first computed tomography (CT) scan date,Tumour size was defined by surgical or imaging staging.

In patients for whom no histology was present, the diagnosis of cancer was based on information from the clinical history, radiology reports and tumor marker measures.

CA19.9 considered significant if it was above upper normal level of our local laboratories (>37 I.U/l). Patients with normal CA19.9 values were excluded from the final analyses.

Initial hospital stay duration was defined as the time spent in hospital after the patient's surgical or endoscopic procedure. Data on short- and longterm morbidity in terms of postoperative complications and hospital readmissions were also collected. Perioperative complications were defined as complications that occur within 30 days after stent insertion or surgical intervention.Thirty day mortality for each group of treatments was calculated. Longterm disease- survival data were collected by either telephoning or from hospital records.

The selection of patients for palliative surgical intervention over endoscopic palliative therapy was based upon patient preference and judged fitness for operative intervention.

Endoscopic Technique :

Patients who undergoing therapeutic self expanding, uncovered metalic stenting ,of 5 cm length and 8 mm width ,usually start with a side-viewing duodenoscope and stenting under fluoroscopic guidance.The position of stent was confirmed by its anatomic location, visualization of bile drainage and injection of contrast into the stent after placement to ensure its position above the bile duct stricture.

Surgical Technique:

All patients undergoing palliative surgery underwent a triple bypass comprising a hepatojejunostomy-Roux-en-Y,side to side anastemosis and gastrojejunostomy,under general anasthesia.

Statistical Analysis;

Data were analysed using SPSS version 11.5 , Median survival was analysed by the log rank test and represented by Kaplan–Meier graphs. Other continuous data of normal distribution were analysed by descriptive analysis with means compared by independent *t*-test. Categorical variables were analysed using Fisher's exact test. A *P*-value of <0.05 was considered statistically significant.

Results:

Within the study period, a total of 60 eligible patients were identified.

Of these, 30 underwent endoscopic stenting and 30 underwent palliative surgery. Follow-up ranged from 1 to 86 weeks,Baseline demographic and haematological values are displayed in Table 5. Patients undergoing palliative surgery have significantly lower CA19.9, inspite of having equivalent tumour sizes. No other values differed statistically between the two groups.

There were no significant differences in immediate complications or mortality rates between patients who underwent palliative stenting and those who underwent palliative surgery (Table 6). Inthe surgical group, the one death was due to respiratory infection complicated by multiple organ failure. In the stent group, causes of death were acute cholangitis ($n = 1$), acute renal failure ($n = 2$), upper GIT bleeding ($n = 1$) and respiratory complications ($n = 1$). After excluding admissions for chemotherapy-related problems (diarrhoea, anemia, or vomiting occurring within 48 hours of treatment) ,the number of readmissions expressed as a percentage of the group population size was greater in stented patients compared with biliary bypass surgery patients (43.3% vs. 10%, respectively) (Fig. 2). The total length of hospital stay per patient was also lower in the surgical bypass group, even including their postoperative stay (34.1 daysvs. 10.2 days). The main causes for readmission were obstruction of bypass and sepsis, which account for 75% of all readmissions. Two patients in endoscopic group developed intractable vomiting, which persisted inspite of discontinuation of chemotherapy, and had imaging evidence of gastric outlet obstruction.

Neither individual proceeded to intervention as they quickly succumbed from advanced disease, Overall survival amongst patients undergoing palliative bypass was significantly greater than in stented patients at 382 days vs. 135 days, respectively (Fig. 3). Preoperative CA19.9 also appeared to influence survival rate: in both groups, patients with CA19.9 values <1000 survived significantly longer than those with CA19.9 >1000 (Fig. 4).

Table 1: Gender distributon of surgical group patients.

Gender	No. and %
male	17(56.6 %)
Female	13(43.4%)
Total	30(100%)

Table 2: Age distribution of surgical group patients.

Age	No. and %
40-49	2(6.6%)
50-59	8(26.7%)
60-69	15(50%)
70-79	5(16.7%)
Total	30(100%)

Table 3: Gender distribution of endoscopic group patients.

Gander	No. and %
Male	14(46.6%)
Female	16(53.4%)
Total	30(100%)

Table 4: Age distribution of endoscopic group patients

Age	No. and %
40-49	4(13.4%)
50-59	7(23.3%)
60-69	12(40%)
70-79	7(23.3%)
total	30(100%)

Table 5: Demographic variables among patients undergoing endoscopic stenting and palliative surgery

	Surgical palliative		Endoscopic stenting	p-value
complication	n=30		n=30	
	sepsis	12(40%)	6(20%)	0.091
	bleeding	3(10%)	5(16.6%)	0.065
	Stent blockage or bypass	NA	3(10%)	NA
Thirty-day mortality	1(3.3%)		5(16.6%)	0.085
Total	16(53.3%)		19(63.3%)	

N.B. T.S.B= Total serum bilirubin

Table 6: Early complications and mortality within 30 days after palliative surgery or endoscopic stenting

Variable	Surgicalgroup (n=30)	Endoscopic Group (n=30)	significance Value
CA-19.9 (I.U/l) median	1100	3870	0.039
T.S.B (mg/dL)median	190	280	0.125
Tumour size (mm)	32	35	0.476

NA;not applicable
N.T 1: (12)septic patiants included,(3)URTI,(3)wound infection,(2)sever UTI,(2) cholangitis,(2) biliary leak.
N.T 2: (6) septic patiants included,(4) pancreatitis,(1) cholangitis,(1) URTI.

Table 7; late complications and mortality after 30 days of palliative surgery or endoscopic stenting

Variable	presentation	Surgical bypass	Endoscopic stenting	P-value
Complication		N0.=30	No.=30	
	Cholengitis	2	2	NS
	Abdominal pain	1	1	NS
	Jaundice recurance	0	8	NS
	G.O.O	0	2	NS
Mortality		0	2	NS
Total		3	15	NS

NS:not significant

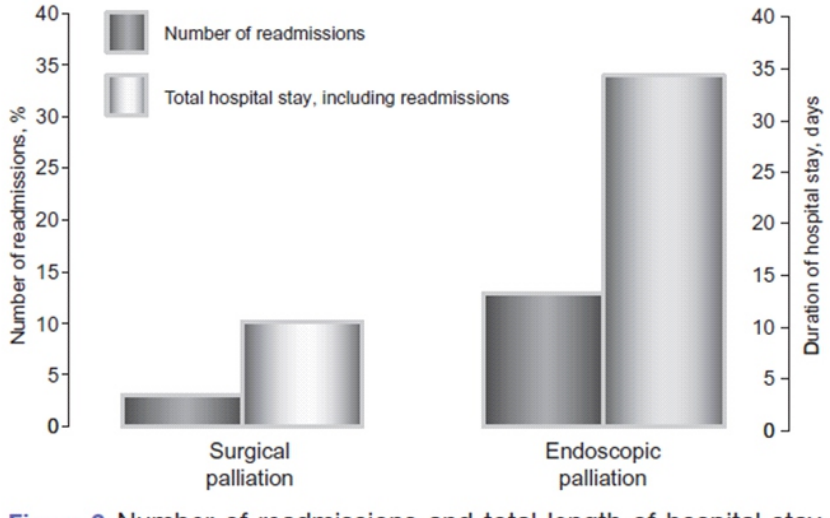


Figure 2 Number of readmissions and total length of hospital stay following palliative surgery and endoscopic stenting, respectively ($P < 0.05$)

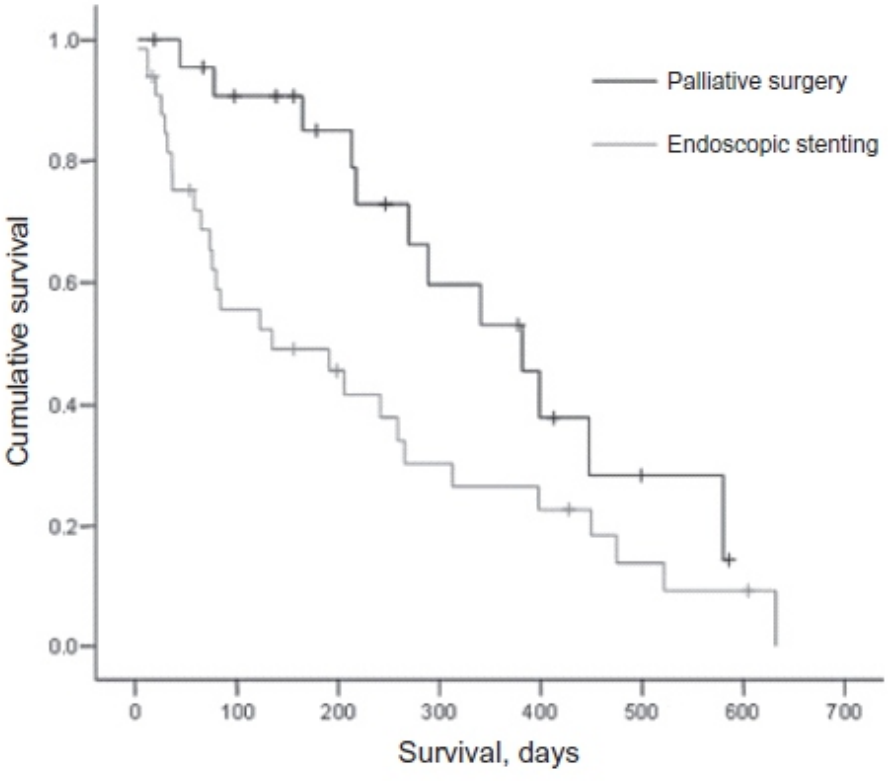


Figure 3 Survival following palliative surgery and endoscopic stenting, respectively ($P < 0.05$)

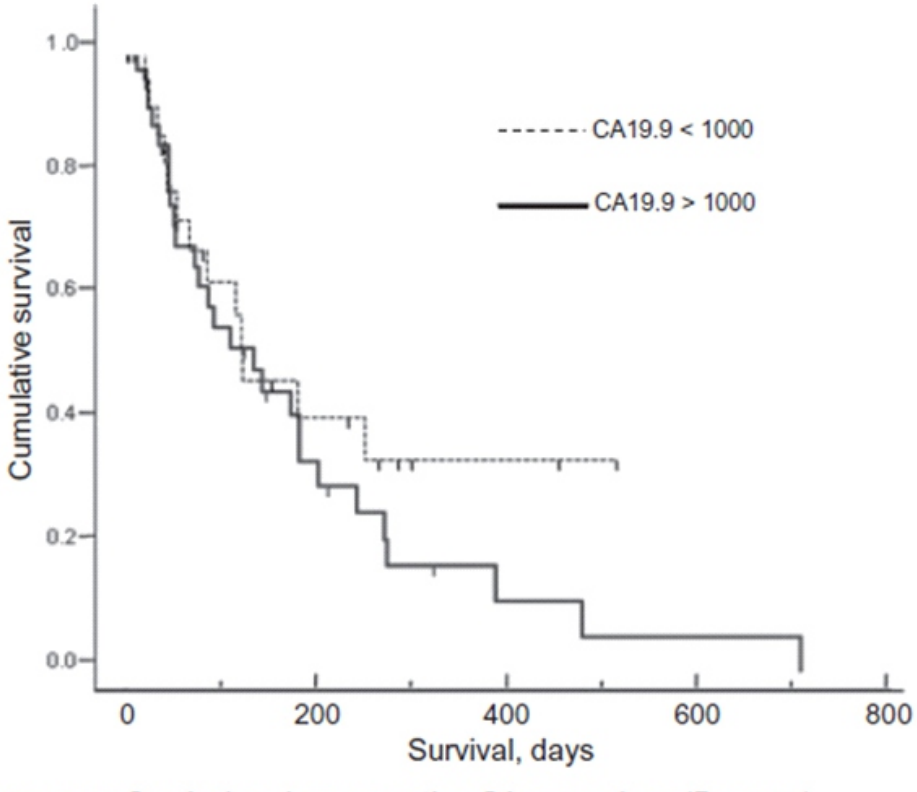


Figure 4 Survival and preoperative CA19.9 values ($P < 0.05$)

Discussion:

Overall, our results suggest that surgical bypass can be performed with lower morbidity and mortality rates to biliary stenting group, in selected patients, but with a significantly lower risk of readmission.

Which is similar to Sunpawervong et al., in 2005[29] found No difference in morbidity between two groups ; and surgical palliation resulted in significantly less common late complications (jaundice), On the other hand, Nuzzo et al., 2004[30] proved Higher incidence of complications and lower quality of life in stented group,which made surgical bypass the treatment of choice,meanwhile, Santagati et al., 2003[31] shows higher complication rate, mortality rate in surgically palliated patients compared to stenting patients, therefore, better palliation could be done in patients who are able to tolerate biliary bypass surgery.

The increased survival observed in the surgical bypass cohort is probably because of a better overall state of fitness, reflected in the lower median age of patients undergoing surgery. In addition, patients who underwent bypass surgery had significantly lower CA19.9 levels than those who underwent endoscopic stenting (Table 1). In this study, we found CA19.9 levels >1000 to be associated with significantly lower survival than levels <1000 (Fig. 4).(p-value<0.05) ,which is similar to Lundin et al, 1994[35]; and Safi et al, 1998[36], thesis, that stated on unfavourable prognosis in high preoperative concentration of CA-19-9,and poor survival rate and perfomance status as mentioned by Ishii et al, 1997[37].

it is possible that patients who underwent endoscopic stenting had a higher occult tumour burden than those with bypass surgery, which surely have negatively affection on their longterm survival.

In our study,The survival rate in patients who underwent bypass may also be influenced by our relatively conservative policy in selection of patients of pancreatic adenocarcinoma and the fact that no patients with distant pancreatic metastases were included in this study. Despite these facts, it is beleivable that avoiding recurrent admissions for jaundice and concurrent sepsis, in surgical bypass may contribute to the increased survival in this group,while Sunpawervong et al., 2005[29] said no differance in survival between endoscopic and surgical bypass groups,and the same results of no differance in survival for both Raikar et al., 1996[21] andAnderson et al., 1989[32].

In our series,there is significance in total length of hospital stay and number of readmission(p-value<0.05) between surgical bypass and endoscopic stenting groups (10.2vs. 34.1 days) and (10.% vs.43.3%) respectively as shown in figure (2),similar to Nuzzo et al., 2004[30] and Shepard et al., 1988[33] that proved more number of readmission in stenting group versus surgical bypass group,but Santagati et al., 2003[31] shows long hospital stay in surgical bypass patiants, in contrast to Maosheng et al., 2001[34] in this thesis ,ashort hospital stay was found in surgical palliative group.

Schwarz *et al.* concluded that an endoprosthesis should be placed if there was evidence of hepatic, peritoneal or pulmonary metastases or if the patient had significant co-morbidity precluding surgery. [38]

In our series, in addition to,surgical bypass can be performed with similar morbidity and mortality rates to endoprosthesis, also it has the same initial hospital stay, and Rates of late complications and readmissions are higher in patients who undergo stenting than in those with biliary bypass.

The published data suggest that biliary stenting should be reserved for those with a shorter expected survival and that surgical palliation should be offered to those patients who are expected to live longer and who are able to tolerate surgical intervention ,The cut-off in survival determining these two treatment modalities has often been quoted at 6 months[13,29,30,34,38].

In addition to anaesthetic considerations, other factors that carry poor

survival in the palliative treatment of pancreatic cancer that not included in our study,these factors include C-reactive protein levels,[39] leucocytosis,[39] duodenal invasion, [40] peritoneal dissemination, [40] high bilirubin, [41]low haemoglobin, [41] low albumin, [41] presence of ascites[42] and the Karnofsky index of performance status.[43],and These factors are useful in selecting cases appropriate for bypass procedures vs.Endoscopic stenting.

During surgical inervention, as part of our policy,is to perform a gastrojejunostomy at the time of a biliary bypass, Because noted that patient who underwent endoscopic palliative stenting of a biliary obstruction may re-presented again with gastric outlet obstruction. So that use of a routine gastrojejunostomy can be performed with no increase in morbidity and mortality and recommending that a gastrojejunostomy and biliary bypass be undertaken as asingle procedure.[14,44,45–49], and The fact that two patients in our study who underwent endoscopic stenting developed gastric outlet obstruction that supports the use of prophylactic gastrojejunostomy in patients undergoing operative intervention. It has been reported that patients with peritoneal seading do not survive long enough to develop gastric outlet obstruction;[50] however, these patients would make poor surgical candidates and are best treated using endoscopic stenting.

The use of selfexpanding metal stents to treat malignant gastroduodenal outlet obstruction raises the possibility of using endoscopic stents solely to palliate advanced pancreatic cancer without the need for bypass[51,52] although it would appear that even these gastrointestinal stents are susceptible to tumour ingrowth.[53] More data are needed to evaluate this further.

The following table shows the summary of multiple studies that compare between surgical bypass and endoscopic stenting;

Study,auther,year	Study type	No. of patients	findings	Study conclusions
Sunpawervong et al; 2005	retrospective	116	No difference in survival time;morbidity;surgical palliation resulted in significantly less common late complications(jaundice)	In favour of surgical palliation
Nuzzo et al;2004	retrospective	84	Higher incidence of complication in stented group with frequent hospital admissions and lower quality of life	In favour of surgical palliation
Santagati et al;2003	retrospective	107	Higher complication rate;mortality rate and hosspital stay in surgical palliated patient	In favour of endoscopic palliation
Maosheng et al;2001	retrospective	Metalic stents	High rate of late complication in metalic stent group,but shorter hospital stay.	In favour of surgical palliation in patients expected to live>6 months
Wanger et al;2000	retrospective	348	-------	In favour of surgical palliation.
Raikar et al;1996	retrospective	66	Endoscopic treatment resulted in shorter hospital stay,with equivalent survival	In favour of endoscopic palliation.
Smith et al;1994	Randomized	204	Lower mortality and complication rates with stenting,but higher rate of late complications	Both effective palliative treatments.
Van den bosch et al;1994	retrospective	148	Higher early morbidity and mortality in surgical bypass,higher late complication with stenting.	Surgical palliation if life exppectency>6 months
Anderson et al;1989	randomized	50	No differences in survival or palliation	In favour of endoscopic palliation
Shepard et al;1988	randomized	52	No difference in overall survival,more readmission in the stented group, but total time in hospital still shorter than in those surgical bypass.	Endoscopic palliation is agood alternative to surgery.
Sonnenfeld et al;1986	retrospective	41	Major complication more common in surgical bypass group with longer hospital stays,no difference in mortality or survival	-----
Bornman et al;1986	randomized	53	Shorter hospital admission in the stented group,but higher rate of readmissions longterm,no difference in survival	--------
Our study	Douple control	60	Surgical bypass have Border line significant morbidity and mortality rates, and equal lenght of initial hospital stay as endoscopic stenting,and that result in lower rate of late complications	In favour of surgical palliation.

Conclusion:

1. The surgical Triple bypass is an efficacious means of palliating patients with locally advanced pancreatic head adenocarcinoma.
2. Published studies suggest that surgical bypass offers a lower rate of late complications, but involves a higher rate of initial complications and a longer hospital stay than stenting procedure. By contrast, we have shown that surgical bypass can be performed with non significant but border line, morbidity and mortality rates ,and equal length of initial hospital stay as endoscopic stenting, and that it results in a lower rate of late complications.
3. Surgical bypass in our series is associated with high survival rate compared with palliative stenting group.

Recommendation:

1. Further more expantion of study,including number of patiants and study peroid in order to get more specific and sensitive results.
2. In well selected patients with optimal operative risk,it is better to perform surgical bypass rather than biliary stenting because of better survival rate and lower rate of late compications.
3. Support palliative surgical bypass over stenting because of short total hospital stay and consequently less cost effectiveness.

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