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Treatment outcomes of pancreatic cancer in the elderly — literature review

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Abstract: Background: The older population is very heterogeneous with regard to the co-morbidity and the physical reserve. This can result in unacceptably high postoperative complications rates. Therefore, the aim of the study was to review the literature regarding the outcomes of older patients treated for pancreatic cancer, including the usage of minimal invasive techniques.
Methodology: A review of the literature was carried out including studies on pancreatic cancer in older patients published between 2011 and 2016.
Results: Seventeen retrospective studies were included. The total number of patients was 9981 with the age range of 65 years and more. Studies on surgical treatment alone (1.4%), neoadjuvant/adjuvant treatment with or without surgery (89.4%) and palliative therapy (9.2%) were assessed separately. Appropriate comparison was difficult due to the retrospective character and heterogeneity of the study population. Mortality was low, yet there was a great difference in morbidity ranging from some percent to even 100% of the study population. Long-term results were poor.
Conclusions: The functional status, not the chronological age alone, is the factor limiting therapeutic options in older patients with pancreatic cancer.

Key words: cancer, pancreas, elderly, outcomes.

Introduction

Pancreatic cancer is the seventh most common cause of cancer-related death worldwide and the incidence rate is increasing [1]. Of the many factors influencing this condition the most important is the ageing of the society. Higher life expectancy gives opportunity to develop cancer disease [2–23].

However, the older population is very heterogeneous with regard to the co-morbidity and the physical reserve, which makes some of them very vulnerable to stressors, such as surgery. This can result in unacceptably high postoperative complications rates. Therefore, it is necessary to provide a comprehensive review of the literature regarding the outcomes of older patients treated for pancreatic cancer.

Materials and Methods

In January 2017, a review of the literature was carried out including studies on pancreatic cancer in older patients published in the Pubmed database between 2011 and 2016. Search words were: "treatment" AND "outcome" AND "pancreatic cancer" AND "elderly" OR "older". To narrow down the search –age (65+), language (English) and species (humans) filters were used. The literature search and study selection is summarized in Fig. 1.

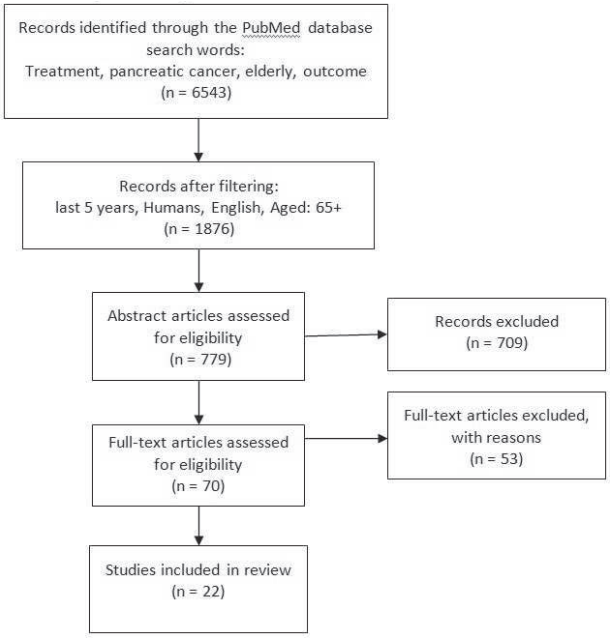

Fig. 1. Flow chart of the study selection process.

Results

In the review, we finally included 22 retrospective studies (including one retrospective analysis of a randomized study) on patients treated between 1990 and 2016. The total number of patients was 9981 in which 5696 (57.1%) were female and 4263 (42.7%) were male. In two studies (33 patients; 0.2% of all included patients) the gender was not mentioned. The median/mean age was not mentioned in most of the papers, but the age range was 65 years and more. Ninety seven percent (9667) of patients had ductal adenocarcinoma, 0.1% (7) neuroendocrine tumour and in 2.9% (307) of cases the tumour type was not mentioned. The characteristics of the included studies were shown in Table 1. Studies on surgical treatment alone, neoadjuvant/adjuvant treatment with or without surgery and palliative therapy were assessed separately.

Table 1. Characteristics of the included studies.

Article/authors	Time of study/ publication year	Type of study	No. of patients	Female/ Male	Mean age (range)
[2] Imaoka *et al.*	2007–2009/2016	Retrospective (on previous randomised trial)	90	37/53	74.0 (NM)
			85	39/46	73.4 (NM)
			86	45/41	73.6 (NM)
[3] Beltrame *et al.*	1998–2011/2015	Retrospective	23	12/11	82.6 (80–86)
[4] Frakes *et al.*	2000–2012/2015	Retrospective	35	18/17	NM (70–75)
			26	15/11	NM (76–80)
			26	10/16	NM (≥80)
[5] Li *et al.*	2005–2013/2015	Retrospective	114	133/104	NM (75–79)
			84		NM (80–84)
			39		NM (≥85)
[6] Jeon *et al.*	2007–2009/2015	Retrospective	7813	4601/3212	NM (≥65)
[7] Kinoshita *et al.*	2005–2012/2015	Retrospective	26	17/9	82 (80–87)
			20	8/12	82 (80–88)
[8] Miura *et al.*	2009–2014/2015	Retrospective	36	15/21	NM (≥75)
[9] Berger *et al.*	2007–2012/2014	Retrospective	53	27/26	73 (70–89)
[10] Cooper *et al.*	2000–2008/2014	Retrospective	179	85/94	NM (≥70)
			57	31/26	
[11] Gangl *et al.*	2001–2010/2014	Retrospective	9	6/3	83 (80–91)
[12] Kanda *et al.*	2000–2012/2014	Retrospective	43	16/27	75 (72–78)
			47	21/26	73.5 (71–76)
[13] Nagrial *et al.*	1990–2011/2013	Retrospective	178	99/79	75.2 (70–87)

Table 1. Cont.

Article/authors	Time of study/ publication year	Type of study	No. of patients	Female/ Male	Mean age (range)
[14] Kizilbash *et al.*	1998–2005/2012	Retrospective	334	177/157	72 (≥65)
			177	89/88	
			169	88/81	
			25	NM	
[15] Marcovalerio *et al.*	1990–2009/2012	Retrospective	25	9/16	83.1 (80–89)
[16] Hatzaras *et al.*	1990–2007/2011	Retrospective	27	13/14	83.4 (80–91)
[17] Hentic *et al.*	2000–2006/2011	Retrospective	20	12/8	78 (75–84)
			18	8/10	
[18] Matsumoto *et al.*	2003–2009/2011	Retrospective	36	20/16	74 (65–86)
			32	10/22	83 (66–96)
[19] Aprea *et al.*	2012–2015/2016 (online)	Retrospective	7	5/2	73.6 (71.1–76.1)
			15	10/5	73.5 (NM)
[20] Fernandez-Cruz *et al.**	2016/2016	Retrospective	11	7/4	73.9 (67–83)
[21] Poves *et al.**	2012–2014/2015	Retrospective	4	3/2	75 (67–78)
[22] Pavlik Marangos *et al.**	1997–2012/2012	Retrospective	14	10/4	73.4 (66–83)
[23] Kendrick *et al.**	2007–2010/2011	Retrospective	8	NM	76.6 (68–81)

* series of case reports, NM — not mentioned.

Outcomes of surgical treatment alone

Ninety nine (1%) patients were treated with surgery alone. There were 50 (50.5%) females and 49 (49.5%) males. The median age was between 73.5 and 83.4 years. The ductal adenocarcinoma was present in 81 (81.8%) of cases and only 3 (3.0%) patients had neuroendocrine tumours. The other patients (15, 15.2%) had unknown histological type of tumours. The location and the stage of the tumour were not given in most of the papers. Seventy-six patients (76.8%) underwent pancreatoduodenectomy, including 26 (26.3%) pylorus-preserving surgery, twenty (20.2%) patients distal or subtotal pancreatectomy and 3 (3.0%) total pancreatectomy. Two (2.0%) patients had concomitant vascular resection. The morbidity range was from 33.3% to 68% of study population. In the postoperative period two deaths (2.0%) were reported as resulting from the procedure. The follow-up period was to 144 months, with mean follow-up period equal to 6 months for one study. Median overall survival range was 10.5–33.3 months. The detailed characteristics of the studies with only the surgical approach are summarized in Table 2. Separate data is shown for minimal invasive

Table 2. Summary of the studies reporting the outcome of the surgery alone.

Article/authors	N (F/M)	Mean age (range)	Histologic type (n)	Location (n)	Stage (n)	Applied treatment (n)	Morbidity (%)	Mortality %(n)	Follow-up time [months]	Median overall survival [months]
[3] Beltrame *et al.*	23 (12/11)	82.6 (80–86)	AdenoCa (23)	NM	NM	Pylorus preserving PD (21) Total pancreatectomy (2) Concomitantvascularre-section (2)	43.0	0.0 (0)	120	19.0
[11] Gangl *et al.*	9 (6/3)	83.0 (80–91)	AdenoCa (9)	NM	AJCC II (8) III (1)	Pylorus-preserving PD (5) PD (1) Distal pancreatectomy (2) Total pancreatectomy (1)	33.3	0.0 (0)	144	10.5
[15] Marcovalerio *et al.*	25 (9/16)	83.1 (80–89)	AdenoCa (25)	NM	AJCC IIA (8) IIB (17)	PD (25)	68.0	4.0 (1)	35	17.3
[16] Hatzaras *et al.*	27 (13/14)	83.4 (80–91)	AdenoCa (24) Neuro--endocrine (3)	Head (25) Body/Tail (5)	NM	PD (20) Distal pancreatectomy/ Subtotal pancreatectomy (5)	52.0	3.7 (1)	60	33.3
[19] Aprea *et al.*	15 (10/5)	73.5 (NM)	NM	NM	NM	Distal pancreatectomy (15)	33.3	0.0 (0)	6 — mean	NM

NM — not mentioned, AdenoCa — adenocarcinoma, AJCC — American Joint Committee on Cancer, PD — pancreatoduodenectomy.

Table 3. Summary of the studies reporting the outcome of minimal invasive techniques.

Article/authors	N (F/M)	Mean age (range)	Histologic type (n)	Location (n)	Applied treatment (n)	Operative time [minutes]	Postoperative hospital stay Mean (range)	Morbidity (%)	Mortality %(n)	Follow-up time [months]
[19] Aprea *et al.*	7 (5/2)	73.6 (71.1–76.1)	NM	Body (2) Tail (5)	Laparoscopic distal pancreatectomy (7)	186.2 ± 11	7.2 (NM)	28.6	0.0 (0)	6 — mean
[20] Fernandez--Cruz *et al.**	11 (7/4)	73.9 (67–83)	AdenoCa (5) NF NET (2) Insulinoma (1) Carcinoid (1) Acinar cell Ca (1) Other (1)	Body-Tail (11)	Laparoscopic en-bloc distal pancreatectomy with splenectomy (11)	114–378	NM (4–30)	NM	9 (1)	80
[21] Poves *et al.**	4 (3/2)	75 (67–78)	AdenoCa (3) NF NET (1)	NM	Laparoscopic en bloc distal splenopancreatectomy and left nephrectomy (1) Laparoscopic spleen-preserving distal pancreatectomy (1) Laparoscopic distal splenopancreatectomy (2)	125–359	4.7 (NM)	25.0	NM	30
[22] Pavlik Marangos *et al.**	14 (10/4)	73.4 (66–83)	AdenoCa (11) Intraductal papillary mucinous neoplasm (3)	NM	Laparoscopic distal pancreatectomy with splenectomy (14)	73–313	5 (NM)	23.0	NM	108
[23] Kendrick *et al.**	8 (NM)	76.6 (68–81)	AdenoCa (NM) NET (NM)	NM	total laparoscopic PD with major venous resection (8)	370–666	NM (4–35)	NM	0.0 (0)	19

NM — not mentioned, AdenoCa — adenocarcinoma, NF NET — non functioning neuroendocrine tumours, PD — pancreatoduodenectomy, * — studies with case report series (no full data for patients 65+).

techniques in Table 3. There were 44 (0.4%) patients treated by laparoscopy: twenty-five females (56.8%), 12 (27.3%) males and 8 patients with unknown gender. The median age was from 73.4 to 76.6 years. Laparoscopic distal pancreatectomy was leading procedure (36, 81.8%) connected with splenectomy (28, 63.6%) and nephrectomy in one case. Eight (18.2%) patients underwent total laparoscopic pancreatoduodenectomy with major venous resection. Operative time for this procedures was between 73 and 666 minutes. In most cases follow-up time was dictated by survival time of patients and it was even to 108 months.

Outcomes of multimodal treatment

The majority of there viewed patients had combined therapy. The detailed characteristics of the studies are summarized in Table 4. There were 8924 (89.4%) patients of which 5137 (57.6%) were female and 3738 (41.9%) male. Two studies (49 patients; 0.5%) did not mention the gender. The age of the included patients was over 65. Based on the American Joint Committee on Cancer classification, there were 1961 (21.9%) stage I–II tumours, and 1037 (11.6%) stage III–IV tumours. More detailed tumour stages were reported in few of the studies. Sixty-six and half percent of patients did not have any information about the stage.

Surgery was the treatment for 1874 (21.0%) patients: pancreatoduodenectomy (847; 45.2%) followed by partial surgery (126; 6.7% not closely defined by the authors), total pancreatectomy (41; 2.2%) and distal pancreatectomy (27; 1.4%). Concomitant vessel resection was performed in 86 (4.5%) patients. In 41% (768) of patients the type of surgery was not mentioned. The treatment was combined with chemotherapy alone in 1914 (21.4%), with chemoradiotherapy in 705 (7.9%) and radiotherapy alone in 606 (6.8%) patients. One study investigated the combination of the surgical treatment with versus without the statins, including 2544 (28.5%) patients.

The morbidity range was reported to be between 42.2% and 100% of the study population, including 35% of patients with major complications. The most common reported complication was pancreatic fistula (41; 0.4%) followed by wound infection (27; 0.3%) and other gastrointestinal problems (16; 0.2%). Seven (0.1%) patients died and 16 (0.2%) were readmitted. The follow-up time was from 48 to 106 months with median overall survival of 2.4–27 months. In case of one patient there was a complete response to the neoadjuvant treatment.

Outcomes of palliative treatment

Nine hundred sixteen (9.2%) patients received palliative treatment: 470 (51.3%) were female and 446 (48.7%) were male. The included patients were 65 or over. In most cases ductal adenocarcinoma was diagnosed (635; 69.3%), but for 281 (30.7%) the

Table 4. Summary of the studies reporting the outcomes of the multimodal treatment.

Article/authors	N (F/M)	Mean age (range)	Location (n)	AJCC Stage (n)	
[4] Frakes *et al.*	35 (18/17)	NM (70–75)	Head (87)	I (5) II (11)	III (70) IV (1)
	26 (15/11)	NM (76–80)			
	26 (10/16)	NM (≥80)			
[6] Jeon *et al.*	5357 (3160/2197)	NM (≥65)	NM	I–II (718) III–IV (640) **Unknown (3999)**	
	2456 (1441/1015)		NM	I–II (432) III–IV (314) **Unknown (1710)**	
[7] Kinoshita *et al.*	26 (17/9)	82 (80–87)	NM	I (2)	II (20) IV (4)
[8] Miura *et al.*	24 (NM)	NM (≥75)	NM	I (9) II (14) Complete response (1)	
[10] Cooper *et al.*	179 (85/94)	NM (≥70)	Head (160) Body/Tail (19)	Primary resectable (153) Borderline (26)	
[12] Kanda *et al.*	43 (16/27)	75 (72–78)	Ductal location (90)	I (1) IIA (15)	IIB (23) IV (2)
	47 (21/26)	73.5 (71–76)		I (2) IIA (10)	IIB (29) IV (6)
[14] Kizilbash *et al.*	334 (177/157)	72 (65+)	Head (258) Body/Tail (76)	I (47)	IIA (84) IIB (203)
	177 (89/88)		Head (144) Body/Tail (33)	I (22)	IIA (38) IIB (116)
	169 (88/81)		Head (121) Body/Tail (48)	I (25)	IIA (35) IIB (107)
	25 (NM)		NM	IIB (13) Others (12)	

NM — not mentioned, PD — pancreatoduodenectomy, AdenoCa — adenocarcinoma, AJCC — American Joint Committee on Cancer, FU — fluorouracil.

Applied treatment (n)		Morbidity (%)	Mortality % (n)	Follow-up time [months]	Median OS [months]
PD + chemoradiotherapy (41)		54.4	0 (0)	60	23.4
PD + chemotherapy (17)		42.2	15.4 (4)		16.1
PD without chemo/radiotherapy (29)		49.9	3.8 (1)		18.7
Unknown resection extend (500) Chemotherapy (998) Radiation therapy (368)		NM	NM	48	2.4
Simvastatin (1184) Atorvastatin (605) Lovastatin (452) Other statins (303)	Unknown resection extend (342) Chemotherapy (637) Radiation therapy (238)	NM	NM		4.7
PD (16) Total pancreatectomy (1) Distal pancreatectomy (9)	Vessel resection (10) + adjuvant chemotherapy (13)	100 (8% Clavien-Dindo over III)	0 (0)	106	12.4
Pylorus-preserving PD (2) PD (16) Distal Pancreatectomy(3) Total Pancreatectomy (3) + adjuvant therapy — gemcitabine(8)		100 (8% Clavien-Dindo over III)	8.4 (2)	48	27.2
Neoadjuvant treatment (153) (30Gy/10fractions or 50.4Gy/28fractions + gemcitabine, 5-FU or capecitabine) Primary surgery (26)	Subsequent surgery (74 from 153) PD (83) Distal pancreatectomy (15) Total pancreatectomy (2) Adjuvant therapy (23)	33 Major complications rate	NM	60	16.4 Post surgery: 27.0
PD (16) Subtotal pylorus-preserving PD (18)	Pylorus-preserving PD (9) Adjuvant chemotherapy (18)	35 Clavien-Dindo III–IV	0 (0)	60	NM
Portal vein resection with: PD (27) Subtotal pylorus-preserving PD (14)	Pylorus-preserving PD (6) Adjuvant chemotherapy (29)	35 Clavien-Dindo III–IV	0 (0)		11.2
5FU + radiotherapy	Total pancreatectomy (12) Radical pancreatectomy (259) Partial surgery (63)	NM	NM	60	19.0
Gemcitabine + radiotherapy	Radical pancreatectomy (141) Total pancreatectomy (9) Partial surgery (27)	NM	NM		17.0
Gemcitabine	Radical pancreatectomy (125) Total pancreatectomy (8) Partial surgery (36)	NM	NM		14.0
5FU mono	Radical pancreatectomy (19) Total pancreatectomy (6)	NM	NM		27.0

exact histologic type of the tumour was not given. Locally advanced tumours were reported in 154 (16.8%) and metastatic disease was present in 434 (47.4%) patients. The stage was unknown for 328 (35.8%) tumours. Chemotherapy was the most common palliative treatment modality. As the first line chemotherapy, gemcitabine alone was used in 294 (32.1%) cases, gemcitabine combined with other regimens in 241 (26.3%)

Table 5. Summary of the studies reporting the outcomes of the palliative treatment.

Article/authors	N (F/M)		Mean age (range)	Histology type (n)	Location (n)	Stage (n)
[2] Imaoka *et al.*	90 (37/53)		74.0 (NM)	AdenoCa or Adenosquamous Ca	Head (33) Body/tail (53) Unn (4)	Locally advanced (23) Metastases (67)
	85 (39/46)		73.4 (NM)		Head (31) Body/tail (47) Unn (8)	Locally advanced (24) Metastases (61)
	86 (45/41)		73.6 (NM)		Head (41) Body/tail (43) Unn (3)	Locally advanced (28) Metastases (58)
[5] Li *et al.*	114	(133/104)	NM (75–79)	AdenoCa	Head (122) Body/tail (112) Unn (22)	Metastatic disease >70%
	84		NM (80–84)			
	39		NM (≥85)			

tumours, S1 alone (Tegafur/gimeracil/oteracil) for 88 (9.6%) patients and other regimens in 131 (14.3%) cases. Moreover, 3.7% of patients received chemoradiotherapy and 0.4% radiotherapy alone. The follow-up period was 36–193 months with median overall survival range of 1.4–21.8 months. The detailed characteristics of the studies with only the palliative approach are summarized in Table 5.

Treatment (n)		Follow-up time [months]	Median overall survival [months]
Gemcitabine + S1(Tegafur/gimeracil/ oteraci)	Second line: (48) The same (12) S1 (11) Gemcitabine (21) Other (4)	36	10.2
S1 (Tegafur/gimeracil/ oteracil)	Second line: (50) The same (6) Gemcitabine + S1 (3) Gemcitabine (38) Other (3)		8.0
Gemcitabine	Second line: (50) The same (10) S1 (34) Gemcitabine + S1 (5) Other (1)		8.5
Gemcitabine: Mono (50) With erlotinib (13) With oxaliplatin (13) With capecitabine(5) With cisplatin (3)	with 5–FU (1) Capecitabine (1) GTX (1) FOLFOX (2) FOLFIRINOX (3) Clinical trial (9)	42	7.9 Without therapy: 1.4
Gemcitabine: Mono (35) With erlotinib (11) with oxaliplatin (6) with capecitabine (6) with carboplatin (1)	withnab-paclitaxel (1) with 5-FU and HAI cisplatin (1) FOLFOX (2) FOLFIRINOX (3) Clinical trial (4) Unn therapy (1)		7.9 Without therapy: 2.5
Gemcitabine: Mono (23) With capecitabine (1)	FOLFOX (1)		7.7 Without therapy: 4.7

Table 5. Cont.

Article/authors	N (F/M)	Mean age (range)	Histology type (n)	Location (n)	Stage (n)
[7] Kinoshita *et al.*	20 (8/12)	82 (80–88)	NM	NM	NM
[8] Miura *et al.*	36 (15/21)	77 (NM)	AdenoCa	NM	Resectable (19) Borderline resectable (17)
[9] Berger *et al.*	53 (27/26)	73 (70–89)	AdenoCa	NM	Metastatic disease (47) Locally advanced (6)
[10] Cooper *et al.*	57 (31/26)	NM (>70)	AdenoCa	Head (50) Body/Tail (7)	Resectable or borderline
[13] Nagrial *et al.*	178 (99/79)	75.2 (70–87)	AdenoCa	Head (146) Body/tail (28)	AJCC I (6) II (169)
[17] Hentic *et al.*	38 (20/18)	78 (75–84)	AdenoCa	NM	Locallyadvanced (15) Metastaticdisease (15)
[18] Matsumoto *et al.*	36 (16/20)	74 (65–86)	AdenoCa	Head (21) Body/Tail (15)	Locallyadvanced (16) Metastatic (20)

AdenoCa — adenocarcinoma, Unn — unknown, 5FU — fluorouracil, AJCC — American Joint Committee on Cancer, * — median survival time.

Treatment (n)		Follow-up time [months]	Median overall survival [months]
Gemcitabine (10) S-1 (3) Gemcitabine+S-1 (6) → second line gemcitabine (2) Gemcitabine+erlotinib (1)		106	11.7*
Neoadjuvant: Chemotherapy alone (2) Chemoradiation (24) Chemotherapy and chemoradiation (10)	**Chemotherapy regimen:** Gemcitabine alone (4) Gemcitabine doublet (2) 5-FU–based doublet (3) FOLFIRINOX (3)	48	9.1
Gemcitabine-based: (43) Gemcitabine mono (22) Gemcitabine/erlotinib (20) Gemcitabine/capecitabine (1)	FOLFIRINOX (4) OFF (3) Capecitabine (1) FOLFOX (2) Second line treatment (21)	78	6.7
Gemcitabine + cisplatin or erlotinib		60	11.0
Adjuvant chemotherapy (53)		193	21.8
No adjuvant chemo (125)			13.1
Adjuvant radiotherapy (4) Palliative chemotherapy (35)			Global 15.8
Gemcitabine (28) (Gemcitabine 1000 mg/m² as a 30-min infusion weekly for 7 out of 8 wk and then for 3 out of 4 wk)	Gemcitabine with oxaliplatin (2) (Gemcitabine 1000 mg/m² as a 100-min infusion on day 1 and oxaliplatin 100 mg/m² as a 2-h infusion on day 2 every 2 wk).	44	8.9
Intravenous GEM infusion of 600–800 mg/m² during a 30-min period on days 1, 8 and 15 of a 28-day cycle		84	7.6

Discussion

Outcomes of surgical treatment

Based on the current literature, the assessment of surgery outcomes in pancreatic cancer treatment is difficult due to the constant progress in medicine and the long study inclusion time (1990–2011) [3, 15–16]. Twenty years time makes a huge difference in anaesthesia and postoperative care. A small group of older patients (1% of the study population) treated just surgically were not consecutive patients but selected. The age alone is not a contraindication to the procedure. Two studies included patients at the age of 90 years and more. However, the selection process in all studies did not take Comprehensive Geriatric Assessment and frailty into account. Moreover, in the published papers there is often lack of data on tumour location [3, 11, 15] and its stage, which makes any comparison almost impossible [3, 11, 16]. There is also a significant difference in reported morbidity between the studies: Gangl *et al.* (33.3%) versus Marcovalerio *et al.* (68%). This should be, in the opinion of the second authors, due to more liberal inclusion process of patients [11, 15]. Isolated deaths can be assumed as a statistical risk and did not dominate in any research, which may be a benefit of a well-chosen group. The very long follow-up time was reported by the Beltrame *et al.* and Gangl *et al.* (120 and 144 months, respectively). However, only Gangl *et al.* showed that one patient in nine survived such a long time [3, 11]. Moreover, there are differences in the preoperative assessment of the patients. Gangl *et al.* excluded patients with Eastern Cooperative Oncology Group 3–4 score and dementia, while in the case of Hatzaras *et al.* an interdisciplinary team was involved in patient care. The high survival rates can also be attributed to the exclusion of patients with potential frailty syndrome [11, 16]. Moreover, despite the fact that the number of performed laparoscopy increases every year, there is still only few research taking into account the minimally invasive techniques with a sufficient amount of data. We obtained only five studies corresponding to search criteria. Furthermore, 4 of them were based on case report series which makes it impossible to collect all data [20–23]. However, it is interesting that despite similar characteristic of groups in those studies operative time have a large discrepancy (73–666 minutes) [22–23]. It can be explained by performed a renal vein interposition graft done in a longer case, but both authors did not comment this short and long operative time [22–23]. Unfortunately, all authors did not provide median overall survival which could be compared with open surgery, but morbidity and mortality seem to be similar [3, 11, 15–16, 19–23]. Aprea *et al.* compared laparoscopy and open surgery receiving shorter operative time (186.2 ± 11 vs. 180.4 ± 7 minutes, respectively), less blood loss (212.30 ± 62 vs. 342.3 ± 104 ml) and shorter postoperative hospital stay (7.2 ± 1.2 vs. 11.3 ± 4 days) [19]. Chapman *et al.* obtained similar data additionally they showed that conversion worsening the

outcome after treatment [24]. Therefore, the operator's experience may be crucial. The learning curve of laparoscopic distal pancreatectomy showed that benefits are higher after 17th operated patient [25].

After the process of selection of articles for review, a meta-analysis concerning pancreatoduodenectomy in pancreatic head tumours in the elderly was published. In this publication Pędziwiatr, Małczak *et al.* presented a similar level of postoperative complications (47.23% vs 33.3% — 68%) in the elderly, while showing a higher level of mortality (4.54% vs 2.0%), which may be due to the small number of groups in our study (number of patient respectively, 2180 vs 99) [26]. Summarising the current literature and mentioned meta-analysis, the chronologic age is not a contraindication to the surgery and in well selected older patients treated in reference centres low morbidity and mortality can be achieved especially with minimal invasive techniques. However, we do not have information on the quality of life of the older patients from articles selected to review, which is often more important than long survival.

Outcomes of the multimodal treatment

The direct comparison is very difficult because in the biggest study [6] we do not have information on tumour stages. Moreover, the authors do not report neoadjuvant/adjuvant regimens applied [4, 6–8, 10, 12]. Only the Kizilbash *et al.* give the complete data [14].

There was a significant difference in the morbidity rate reported by the authors: from 33% to even 100%. However, in the later study (with 100% morbidity) there were only 8% of major complications defined as Clavien-Dindo III or greater [7–8]. Despite this, Kinoshita *et al.* and Miura *et al.* did not assess the quality of life (during and after treatment), which may be more important than achieving null mortality [7–8].

Jeon *et al.* examined anti-cancer properties of statins shown in mechanistic studies [6]. The significantly lower median survival time observed in this study is difficult to comment on due to unknown tumour stage and lack of information on treatment. In most cases patients were using only statins without additional treatment. Summarising this study, statins reduced death rates by 7–9% but only for grade I–II tumours and in those who underwent surgery, prolonging the survival from 2.4 mo to 4.7 mo [6].

Generally, the age is not a contraindication and a well-chosen group may gain strong benefits from multimodal therapy compared to chemotherapy alone (27 months vs. 16.4 months) [10], especially when it is used prior to surgery (overall survival 27.2 months vs. 9.1–9.7 months) [8]. Beginning with the adjuvant treatment

could be difficult in older patients after surgery due to the general status of the patients and complications of the surgical treatment. In Kinoshita *et al.*'s study only 6 in 26 patients finished the treatment [7] and two thirds of patients in Miura *et al.*'s study [8]. However, most of the studies do not report any use of Geriatric Assessment in the treatment process.

Outcomes of palliative treatment

The great majority of patients had metastatic disease at the moment of the diagnosis; therefore the only solution for increasing the survival of older population may be palliative treatment (Table 5). The combinations of chemotherapeutics provide different types of treatment based mostly on gemcitabine or S1 (Tegafur/gimeracil/oteracil) [2, 5, 7–10, 13, 17–18]. However, many chemotherapeutics have not been tested in older patients with cancer due to the potential detrimental effect on their health [2].

In some studies it is difficult to assess the outcome for lack of control groups without any treatment [7–8, 10]. It is important to realize that patients undergoing palliative therapy are often in a much worse condition. Median overall survival was from 2.5 months to even 21.8 months, which may be promising for palliatively treated patients. Nagrial *et al.* showed evident benefits of receiving palliative treatment (21.8 months vs.13.1 months). However, this study did not show any specific reason for the lack of treatment in the second group [13].

Conclusion

The functional status, not the chronological age alone, is the factor limiting therapeutic options in older patients with pancreatic cancer. The mortality and morbidity in reference centres are low. However, currently published studies are in most cases retrospective and with a great heterogeneity of the included patients, which limits the evidence based decision taking. Therefore, proper Geriatric Assessment of older patients, preferably by a multidisciplinary team, including a geriatrician, should be a key preoperative step. Moreover, prospective studies should be carried out focusing not only on survival but also on the quality of life, which is often more important for older patients. Also, use of minimally invasive techniques should be properly examined in prospective studies, to provide sufficient data about outcomes of treatment.

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