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Research article

Prognostic significance of poorly cohesive gastric carcinoma in Tunisian patients

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ABSTRACT

Background: While the incidence of gastric cancer has decreased worldwide in recent decades, the incidence of poorly cohesive carcinoma (PCC) is rising. The prognostic significance of gastric PCC remains a subject of debate.
Objective: To analyze the prognosis of gastric PCC in a Tunisian cohort.
Methods: A total of 122 gastric adenocarcinoma patients who underwent curative gastrectomy from 2001 to 2014 at Habib Thameur hospital in Tunis, Tunisia were included. The clinicopathological parameters and prognosis of PCC were analyzed in comparison with non PCC (NPCC).
Results: Sixty one patients (50%) presented PCC. Patients were younger in PCC group ($p = 0,001$). There was no difference in sex distribution between the two groups. PCC was more likely to be stage T4 (55.7% vs 34.4%; $p = 0.033$), N3 (67.8% vs 30%; $p < 0.001$) and have a higher metastatic lymph node ratio ($p < 0.001$). Hepatic metastases were more frequent in NPCC group ($p = 0.031$) whereas peritoneal carcinomatosis was more common in PCC group ($p = 0.004$). Perineural invasion was more frequent in PCC group ($p = 0.001$). Resection margins were more often positive in PCC group (31.1% vs 9.8%; $p = 0.004$). There was no difference in recurrence rate between the 2 groups ($p = 0.348$). The 5-year survival was similar in the NPCC and PCC (respectively 43% vs 23 %; $p = 0.247$). Survival rates were also comparable in early stage (100% vs 80% respectively for PCC and NPCC; $p = 0.527$) as well as for advanced stage (16% vs 35% respectively for PCC and NPCC; $p = 0.538$). PCC was not a prognostic factor for survival. Interestingly, advanced age, adjacent structures invasion, positive resection margins were specific prognostic factors for PCC.
Conclusion: In our study PCC was not a prognostic factor for survival. Advanced age, adjacent structures invasion and positive resection margins were specific prognostic features for this histological subtype.

1. Introduction

Gastric cancer is a common tumor that represents the 3rd global cause of death by cancer. Its annual incidence has significantly decreased, but it remains the fifth cancer in the world [1]. In Tunisia, while its incidence has also decreased between 1994 and 2009, it's still a major health public problem: it represents 5% of all cancers, the first digestive cancer in men and the third in women. At diagnosis tumor is metastatic in half of cases. Histologically, adenocarcinoma (ADK) is the predominant type but we observed an increase in the incidence of PCC subtype in the last years [2].

The prognostic significance of histological subtype remains unknown. Indeed, while the poor impact of diffuse histological subtype of Lauren's classification is now well established [3], the prognosis of poorly cohesive carcinoma (PCC) is better [4, 5], equivalent [6, 7] or worse [8, 9] than non PCC (NPCC). Furthermore, PCC appears to be resistant to chemotherapy [9, 10], whereas peri-operative chemotherapy currently represents the therapeutic strategy reference for all gastric

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adenocarcinoma. In Tunisia, no study on the prognostic significance of histologic subtype was conducted until now.

The aim of our study was to compare the PCC and NPCC prognosis and to determine predictive factors of survival in PCC in a Tunisian cohort.

2. Methods

2.1. Study landscape

A retrospective comparative monocentric study in the department of pathology of Habib Thameur Hospital during a period of 14 years (2001–2014) was conducted.

2.2. Study design

- **Inclusion criteria:** A total of 122 patients with histologically proven gastric ADK, who underwent curative or palliative gastrectomy between 2001 and 2014 at the Habib Thameur hospital in Tunis, Tunisia were included.
- **Exclusion criteria:** ADK involving gastro-esophageal junction were excluded from the study.
- **Management of patients:** Pre-operative assessment included a complete medical history, physical examination, upper gastro-intestinal endoscopy with biopsies and computed tomographic scans. Gender, age, tumor size, tumor location, gross appearance, venous, perineural, or lymphovascular invasion, histological classification according to world health organization (WHO), TNM stage according to the 8th edition of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) [11], type of surgery, associated resection and adjuvant chemotherapy were recorded. Linitis was defined macroscopically as partial or complete thickening and rigidity of the gastric wall observed on both pre-operative endoscopy and intra-operative exploration. Pre-operative malnutrition was defined as a weight loss exceeding 10 % of the baseline weight in the last six months.
- **Histologic diagnostic criteria:** PCC, as defined by the 2010 WHO classification, includes the signet ring cell carcinoma. It also includes other forms of carcinoma where tumor cell looks like histiocytes, lymphocytes or cells with highly eosinophilic cytoplasm. Some cells may have irregular and bizarre nuclei [12].
- **Statistical analysis:** A comparative analysis between PCC and NPCC was performed. Survival and predictive factors of survival were analyzed. Univariate analysis aimed to determine dependent prognosis factors. Qualitative variables were compared using the chi-square test or Fisher's exact test. Quantitative variables were compared by the independent Student-t test. Survival was analyzed by Kaplan–Meier method and included postoperative deaths. The log-rank test was used to compare survival curves. Multivariate analysis aimed to determine independent prognosis factors. It was performed by linear regression by Cox proportional hazards stepwise procedure, including non redundant variables chosen by univariate analysis. All statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). A p value ≤ 0.05 was considered statistically significant.
- **Ethics:** Ethical committee approval of Habib Thameur hospital was obtained (approval number: HTHEC-2018-06). No signed informed consent was obtained by patients due to retrospective collect of data. However, patient's confidentiality was respected according to ethical guidelines.

3. Results

3.1. Clinicopathologic findings

Patients'clinicopathological features are detailed in Table 1. Of the 122 patients included in the study, 61 (50%) had PCC. Age at initial diagnosis was younger in PCC group (PCC: 57 years; NPCC: 65 years; $P = 0.001$). Both groups were predominantly of male gender.

Intestinal metaplasia and dysplasia were less present in PCC; however, desmoplasticstroma was more prominent in PCC. Similarly, linitis and perineural invasion were more frequent in PCC. A higher proportion of patients with PCC presented with T4 stage (PCC: 55.7%; NPCC: 34.4%; $p = 0.033$) and N3 (PCC: 65.6%; NPCC: 29.5%; $p < 0.001$). PCC was more likely to present at an advanced AJCC stage (stages 3 and 4). Peritoneal carcinomatosis was more frequent in PCC group ($p = 0.004$); however, hepatic metastases were more frequent in NPCC group ($p = 0.031$). Finally, the rate of complete resection was lower in PCC group. There was no significant difference in recurrence rate between the two groups.

3.2. Overall survival analysis

The 1-year, 3-year and 5-year survival rates of PCC patients were 70.7%, 31.8% and 22.6%, respectively. The 1-year, 3-year and 5-year survival rates of NPCC patients were 68.3%, 55.8% and 43.2%,respectively. There was no significant difference in the overall survival rate between patients with PCC and those with NPCC ($p = 0.241$) (Figure 1).

3.3. Univariate analysis

In PCC group, the 5-year survival rate was influenced by age, malnutrition, tumor size, tumor location, involvement of adjacent organs, extent of gastrectomy, postoperative chemotherapy, TN stage, distant metastasis, peritoneal dissemination, lymphatic invasion, and complete resection (R0) (Table 2). Age >60 years (Figure 2), malnutrition, involvement of adjacent organs, extent of gastrectomy, postoperative chemotherapy and lymphovascular invasion were specific prognostic factors for PCC. Linitis, postoperative complication and perineural invasion were prognostic factors associated with survival in NPCC group.

3.4. Multivariate analysis of Cox proportional hazards regression model

Multivariate Cox proportional hazards models included variables associated with survival in PCC and NPCC group. Age > 60 years, invasion of adjacent organs, incomplete resection, and depth of invasion were specific significant independent prognostic factors in PCC group. However postoperative complication was a significant prognostic indicator only in NPCC group. Over all patients presenting gastric ADK, the Cox proportional hazards model showed that age > 60, invasion of adjacent organs, incomplete resection, depth of invasion, lymph node metastasis and distant metastasis were significant prognostic factors. PCC histology type was not a prognostic factor on multivariate analysis in our cohort (Table 3).

4. Discussion

4.1. Pronostic value of PCC

Based on the analysis of a cohort of 122 patients with gastric ADK, we didn't find a pejorative prognostic value of PCC histological subtype on overall survival. PCC has not been identified as poor prognostic factor neither in univariate nor in multivariate analysis. Interestingly, we found that advanced age, adjacent structures invasion and positive resection margins are specific prognostic factors in PCC. To the best of our knowledge, this was the first Tunisian study that focused on prognostic significance of gastric PCC.

Despite the improvement of the diagnostic means and the therapeutic management of gastric carcinoma, its prognosis remains poor and five-year survival rate, all stages combined, is of 25% [13]. This may be explained by the steady increase in the incidence of PCC which accounts for up to 50% of gastric carcinomas [9] and whose prognosis is supposed to be poor. However, few studies support this hypothesis, like ours. Published data about the prognostic value of different

Table 1. Clinicopathological features of patients stratified according to histologic subtype (PCC vs NPCC).

Variable	All patients (n = 122; %)	PCC group (n = 61; %)	NPCC group (n = 61; %)	P
Gender				0.356
Male	73 (59.8)	34 (55.7)	39 (63.9)	
Female	49 (40.2)	27 (44.3)	22 (36.1)	
Age (years)				
Mean	61.7	57.57 ± 13.54	65.87 ± 12.61	**0.001**
≤60	59 (48.4)	39 (63.9)	20 (32.8)	**0.001**
>60	63 (51.6)	22 (36.1)	41 (67.2)	
Malnutrition				0.781
No	28 (23)	15 (24.6)	13 (21.3)	
Yes	89 (73)	45 (73.7)	44 (72.1)	
Missed data	5 (4)	1 (1.7)	4 (6.6)	
Tumor size (cm)				
Mean	6.6	6.68 ± 3.07	6.53 ± 3.25	0.802
≤5	44 (36.1)	20 (32.8)	26 (42.6)	0.291
>5	68 (55.7)	39 (63.9)	34 (55.8)	
Missed data	10 (8.2)	2 (3.3)	1 (1.6)	
Macroscopic type				0.111
Ulcerated or depressed	38 (31.1)	24 (39.3)	14 (22.9)	
Protruded	78 (64)	33 (54.1)	45 (73.8)	
Flat or slightly elevated	5 (4.1)	3 (5)	2 (3.3)	
Missed data	1 (0.8)	1 (1.6)	0	
Linitis	17 (13.9)	15 (24.6)	2 (3.3)	**0.001**
Tumor location				0.683
Body	60 (49.2)	30 (49.2)	30 (49.2)	
Antrum	58 (47.5)	28 (45.9)	30 (49.2)	
Whole stomach	4 (3.3)	3 (4.9)	1 (1.6)	
Involvement of adjacent organs	24 (19.7)	11 (18)	13 (21.3)	0.580
Gastrectomy				0.440
Total	82 (67.2)	43 (70.5)	39 (63.9)	
Subtotal	40 (32.8)	18 (29.5)	22 (36.1)	
Number of lymph nodes retrieved				0.220
≤16	33 (27)	14 (23)	19 (31.1)	
<16-25≤	40 (32.8)	24 (39.3)	16 (26.2)	
>25	49 (40.2)	23 (37.7)	26 (42.6)	
Postoperative complication	24 (19.7)	12 (19.7)	12 (19.7)	0.920
Postoperative chemotherapy	40 (32.7)	21 (34.4)	19 (31.1)	0.579
Lymphovascular invasion	99 (81.1)	49 (80.3)	50 (82)	0.783
Perineural invasion	90 (73.8)	53 (86.9)	37 (60.7)	**0.001**
Stroma				**<0.001**
Desmoplasia	37 (32.2)	29 (48.3)	8 (14.5)	
Inflammatory microenvironment	78 (67.8)	31 (51.7)	47 (85.5)	
Epithelial abnormality				**<0.001**
Metaplasia	66 (57,9)	22 (36.1)	44 (72.1)	
Dysplasia	16 (14)	2 (3.3)	14 (23)	
Resection				**0.004**
complete (R0)	97 (79.5)	42 (68.9)	55 (90.2)	
incomplete (R1-R2)	25 (20.5)	19 (31.1)	6 (9.8)	
pT stage				**0.033**
T1	11 (9)	2 (3.3)	9 (14.8)	
T2	7 (5.7)	4 (6.6)	3 (4.9)	
T3	49 (40.2)	21 (34.4)	28 (45.9)	
T4	55 (45.1)	34 (55.7)	21 (34.4)	
pN stage				**<0.001**
N0	30 (24.6)	14 (23)	16 (26.2)	
N1	20 (16.4)	3 (4.9)	17 (27.9)	
N2	14 (11.5)	4 (6.6)	10 (16.4)	
N3	58 (47.5)	40 (65.6)	18 (29.5)	

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Table 1 (*continued*)

Variable	All patients (n = 122; %)	PCC group (n = 61; %)	NPCC group (n = 61; %)	P
pM stage				0.185
M0	96 (78.7)	45 (73.8)	51 (83.6)	
M1	26 (21.3)	16 (26.2)	10 (16.4)	
pTNM stage				**<0.001**
Stage I	13 (10.7)	5 (8.2)	8 (13.1)	
Stage II	30 (24.6)	11 (18)	19 (31.1)	
Stage III	53 (43.3)	29 (47.5)	24 (39.3)	
Stage IV	26 (21.3)	16 (26.2)	10 (16.4)	
Peritoneal carcinomatosis	17 (13.9)	14 (23)	3 (4.9)	**0.004**
Hepatic metastasis	8 (6.5)	1 (1.6)	7 (11.5)	**0.031**
Recurrence	33 (27)	18 (27.7)	15 (23.1)	0.348
Peritoneal	23 (18.5)	14 (77.7)	9 (60)	0.234
Loco-regional	9 (7.3)	5 (27.7)	4 (26.6)	0.627
Distant	21 (17.2)	11 (61.1)	10 (66.6)	0.741

PCC, poorly cohesive carcinoma; NPCC, non poorly cohesive carcinoma.
P value significant if lower than 0.05.

histological subtypes of gastric carcinomas appears contradictory and seems to be influenced by the classification used (Lauren classification [14], WHO classification [12] or other classifications) and tumor stage (early or advanced).While the pejorative nature of the diffuse gastric carcinoma of the Lauren classification [3, 14] is confirmed, the prognostic value of PCC in the WHO classification remains controversial [4, 5, 6, 7, 8, 9, 15, 16, 17]. In fact, in accordance with our results, a study carried out by Taghavi et al. in 2012 on 10246 patients with gastric ADK enrolled from 17 cancer registries found no association between PCC histological subtype and survival rate [6]. This result was confirmed by Shim et al. in 2014 on a cohort of 2643 patients [16]. Indeed, in Asian studies that included only gastric ADK [4, 5, 7, 17, 18, 19], it is reported that the survival rate of patients in PCC group is better than that of NPCC group [5, 20, 21]. PCC histological subtype has even been recently identified as an independent factor of good prognosis [5, 23]. This was explained by the fact that the majority of superficial PCC is stage T1a and associated with weak lymph node metastases. Recent studies found that PCC is often discovered at early stage because it gives more ulcerated forms on endoscopy which is easily recognizable [5, 16, 17, 22]. In our study, the 5-year survival of the early PCC group was better than in NPCC group, but the difference was not significant (100% vs. 80%; p = 0.52). However, for patients with advanced gasrtic carcinoma, the prognostic value of histological subtype remains controversial [4, 5, 6, 7, 15, 19, 23]. Many studies have shown that advanced stage PCC gives more parietal invasion (in our study: pT4: PCC = 55,7% vs NPCC = 34.4%; p = 0.033), more lymph node metastases [53,143,145,148], more incomplete surgical resection [8, 17, 21, 24, 27] (in our study, R1/R2: PCC = 31.1% vs NPCC = 9.8%; p = 0.004). However, almost all them, failed to identify PCC subtype as an independent poor prognostic factor.

4.2. Survival analysis

Some studies found that 5-year survival rate appears to be better in patients with PCC [6, 15]. They explain these results by the fact that patients with PCC are often younger with less comorbidity and less postoperative

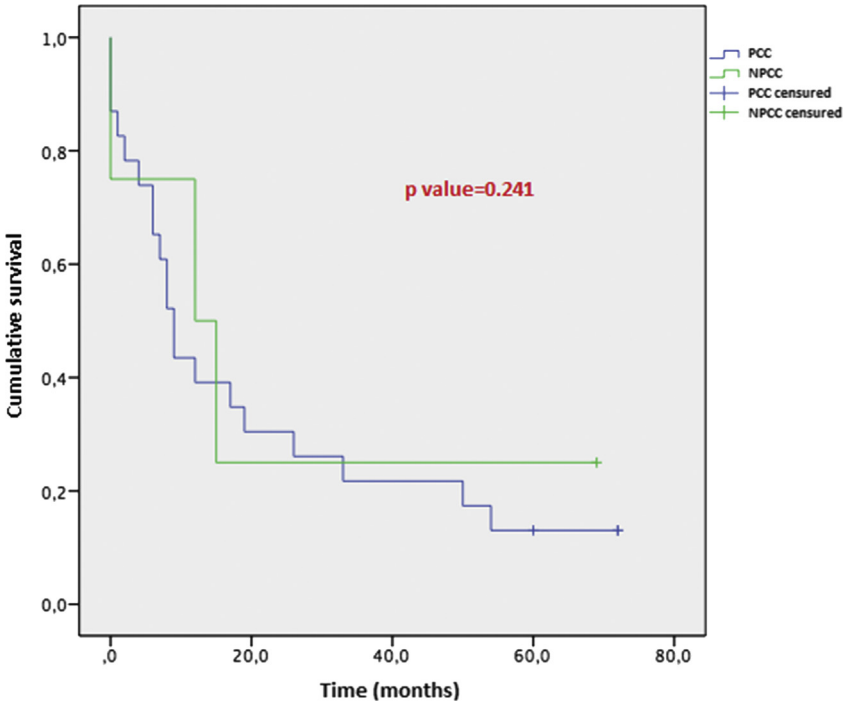

Figure 1. Survival curves in patients with PCC and NPCC.

Table 2. Univariate analysis of factors influencing the overall survival in PCC and NPCC groups.

Variable	All patients			PCC group			NPCC group		
	Number (%)	5 year survival (%)	P	Number (%)	5 year survival (%)	P	Number (%)	5 year survival (%)	p
Gender			0.623			0.272			0.478
Male	54 (61.4)	37.5		23 (53.5)	36.6		31 (68.8)	38.4	
Female	34 (38.6	25.3		20 (46.5)	10.6		14 (31.2)	52.4	
Age (years)			0.248			**0.003**			0.978
≤60	48 (54.5)	32.4		31 (72.1)	27.7		17 (37.7)	42.8	
>60	40 (45.5)	31.8		12 (27.9)	8.3		28 (62.3)	43.5	
Malnutrition			**0.017**			**0.021**			0.268
No	20 (22.7)	56.4		11 (25.6)	50.6		9 (20)	62.5	
Yes	66 (75)	24.2		32 (74.4)	16.1		34 (75.5)	35.2	
Missing data	2 (2.3)						2 (4.5)		
Tumor size (cm)			**0.044**			0.278			0.125
≤5	36 (40.9)	42.3		17 (39.5)	37.8		19 (42.2)	46.8	
>5	52 (59.1)	25.5		29 (60.5)	9		26 (57.8)	41.5	
Linitis			**0.051**			0.227			**0.002**
No	79 (89.8)	36.7		35 (81.4)	30		44 (97.7)	44.2	
Yes	9 (10.2)	0		8 (18.6)	0		1 (2.3)	0	
Tumor location			**0.004**			**<0.001**			**0.008**
Body	42 (47.7)	48.6		20 (46.5)	53.7		22 (48.9)	45.1	
Antrum	43 (48.9)	18.5		21 (48.8)	0		22 (48.9)	44.3	
Whole stomach	3 (3.4)	0		2 (4.7	0		1 (2.2)	0	
Invasion of adjacent organs			**0.092**			**<0.001**			0.629
No	73 (82.9)	34.5		38 (88.4)	25		35 (77.7)	45.9	
Yes	15 (17.1)	*		5 (11.6)	0		10 (22.3)	*	
Gastrectomy			0.059			**0.003**			0.587
Total	60 (68.2)	37.3		31 (72)	35.6		29 (64.4)	42.8	
Subtotal	28 (31.8)	23.7		12 (28)	0		16 (35.6)	44.6	
Number of lymph nodes retrieved			0.074			0.093			0.340
≤16	24 (27.3)	22		11 (25.6)	12.1		13 (28.9)	28.8	
<16–25≤	28 (31.8)	43.6		15 (34.8)	47.3		13 (28.9)	43.1	
>25	36 (40.9)	31.1		17 (39.6	14.6		19 (42.2)	69.7	
Postoperative complication			**0.016**			0.401			**0.007**
No	71 (80.7)	34.1		34 (79)	22.4		37 (82.2)	45.7	
Yes	17 (19.3)	26.5		9 (21)	27.8		8 (17.8)	25	
Postoperative chemotherapy			0.347			**0.036**			0.483
No		39.8			40.8			36.9	
Yes		27			13			48.5	
Lymphovascular invasion			**0.005**			**0.004**			0.141
No	20 (22.7)	61.6		10 (23.2)	65.6		10 (22.2)	55.6	
Yes	68 (77.3)	24.7		33 (76.8)	0		35 (77.8)	40.2	
Perineural invasion			**0.001**			0.062			**0.016**
No	25 (28.4)	66.3		6 (13.9)	60		19 (42.2)	71	
Yes	63 (71.6)	20.2		37 (86.1)	16		26 (57.8)	24.4	
Stroma			**0.050**			0.458			**0.045**
Inflammatory microenvironment	57 (68.7)	37.2		23 (54.7)	30.6		34 (82.9)	41.9	
Desmoplasia	26 (31.3)	*		19 (45.3)	*		7 (17.1)	0	
Resection			**<0.001**			**<0.001**			**<0.001**
complete (R0)	73 (82.9)	39		33 (76.7)	28.3		40 (88.8)	49.6	
incomplete (R1-R2)	15 (77.1)	0		10 (23.3)	0		5 (11.2)	0	
Peritoneal carcinomatosis			**<0.001**			**0.008**			**0.021**
No	75 (85.3)	38.5		32 (74.5)	29.8		43 (95.6)	45.7	
Yes	13 (14.7)	0		11 (25.5)	0		2 (4.4)	0	
pT stage			**<0.001**			**0.023**			**<0.001**
T1	10 (11.4)	85.7		2 (4.6)	100		8 (17.8)	80	
T2	7 (7.9)	68.6		4 (9.3)	75		3 (6.6)	66.7	
T3	33 (37.5)	31.7		16 (37.3)	0		17 (37.8)	66.8	
T4	38 (43.2)	*		21 (48.8)	*		17 (37.8)	*	

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Table 2 (*continued*)

Variable	All patients			PCC group			NPCC group		
	Number (%)	5 year survival (%)	P	Number (%)	5 year survival (%)	P	Number (%)	5 year survival (%)	p
pN stage			**<0.001**			**<0.001**			**0.001**
N0	28 (31.8)	75.4		13 (30.3)	53.7		15 (33.3)	93.3	
N1	13 (14.8)	34.1		2 (4.7)	50		11 (24.5)	24.6	
N2	11 (12.5)	0		3 (6.8)	*		8 (17.7)	0	
N3	36 (40.9)	5.3		25 (58.2)	*		11 (24.5)	12.1	
pM stage			**<0.001**			**0.002**			**<0.001**
M0	70 (79.5)	41.5		31 (72.1)	30.9		39 (86.6)	50.8	
M1	18 (20.5)	0		12 (27.9)	0		6 (13.4)	0	
pTNM stage			**<0.001**			**<0.001**			**<0.001**
Stage I	13 (14.7)	67.1		5 (11.6)	80		8 (17.7)	87.5	
Stage II	24 (27.3)	52.1		10 (23.2)	30.9		14 (31.1)	67.5	
Stage III	33 (37.5)	11.3		16 (37.3)	*		17 (37.8)	19.4	
Stage IV	18 (20.5)	0		12 (27.9)	0		6 (13.4)	0	
Histology									
PCC	43 (48.8)	22.6	0.241						
NPCC	45 (51.2)	43.2							
NPCCC well differentiated	20 (22.7)	48.8	0.254						

PCC, poorly cohesive carcinoma; NPCC, non poorly cohesive carcinoma.
*Censored case number does not allow an accurate estimation of survival.
P value significant if lower than 0.05.

complications compared to the NPCC group. In our study, the PCC group was, on average, 10 years younger than the NPCC group ($p = 0.001$). Similarly, postoperative complications was an independent factor of poor prognosis only for NPCC group (HR = 4.8, 95% CI: 1.46–16.08, $p = 0.010$). The 5-year survival rate of the advanced PCC group was lower compared to the group of NPCC but with no significant difference (16% vs 35%, $p = 0.538$).Interestingly, we found some differences in prognostic factors between the two groups. Indeed, age> 60 years, invasion of adjacent organ, incomplete resection, the pT and pM stages were independent prognostic factors significantly decreasing survival in PCC group. Postoperative complications, pN and pM stages were independent prognostic factors significantly decreasing the survival in the NPCC group. In our cohort, there was no significant difference between PCC group and NPCC group regarding recurrence (27.7% vs. 23.1%). PCC recurred as peritoneal carcinomatosis in 77.7% and as distant metastases in NPCC in 66.6% with no significant difference. It is actually advised to perform a first exploratory laparoscopy to search cancer cells in the peritoneum in PCC. Prophylactic Hyperthermic Intra-peritoneal Chemotherapy (HIPEC) is currently widely used in PCC since peritoneal carcinomatosis worsen prognosis [25, 26]. Furthermore, PCC seems to be less chemosensitive than NPCC and recent studies suggest that it would have a specific sensitivity profile to taxanes and anti-angiogenic agents [9, 27, 28, 29]. In our study, we have interestingly found that survival

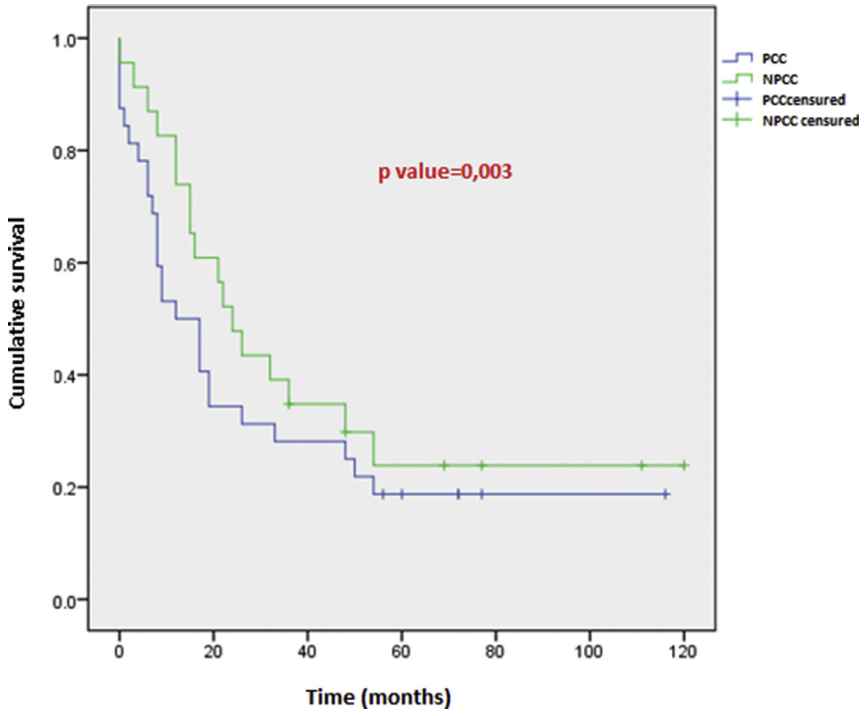

Figure 2. Survival curves in patients aged above 60 years with PCC and NPCC.

Table 3. Multivariate analysis of overall survival.

Variable	All cases			PCC group			NPCC group		
	HR	IC95%	P	HR	IC95%	P	HR	IC95%	P
Age > 60	2.90	1.25–6.73	0.013	6.44	1.71-24.19	0.006			
Invasion of adjacent organs	3.02	1.18–7.70	0.021	40.31	4.15–390.78	0.001			
Incomplete resection	5.72	2.16–15.08	<0.001	28.02	5.19–151.17	<0.001			
pT	2.52	1.34–4.76	0.004	3.74	1.35-10.31	0.011			
pN	3.27	1.74–6.13	<0.001				1.72	1.07-2.77	0.025
pM	3.03	1.14–8.07	0.026	5.99	1.65-21.76	0.006	3.30	1–10.91	0.049
Postoperative complication							4.84	1.46–16	0.010

rate of chemotherapy group was significantly lower than the one with no chemotherapy suggesting that chemotherapy may worsen the prognosis of PCC. Thus it should be managed differently. In addition, although peri-operative chemotherapy is recommended in all gastric carcinomas from stage IA, its interest in PCC remains to be proven. In our study, no patient received peri-operative chemotherapy because it was not available. In fact, chemotherapy is frequently retarded because only one oncology centre is available in our country. Patients are therefore surgically managed.

In conclusion, because of its carcinogenesis, epidemiology, clinical aspects, pathological, molecular and genetic features, gastric PCC should be considered as a distinct pathology among gastric carcinomas. This type of tumor presented specific prognostic factors in our study. Nevertheless, large multicentric studies will help to improve our knowledge about this deadly cancer and its management.

Declarations

Author contribution statement

R. Jouini: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

A. Gharsallah: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

H. Zaafouri: Conceived and designed the experiments; Analyzed and interpreted the data.

A. Debbiche: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

F. Khanchel and I. Helal: Performed the experiments.

M. Sabbah, E. Ben Brahim and D. Hadded: Analyzed and interpreted the data.

M. Ferchichi: Contributed reagents, materials, analysis tools or data.

A. ben Maamer: Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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