CLINICAL, EPIDEMIOLOGICAL AND MOLECULAR PROFILE OF BRAZILIAN PATIENTS WITH PANCREATIC CANCER

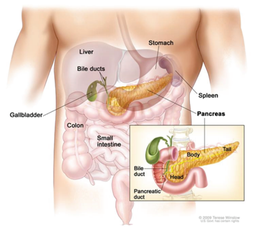
Guaraldi S[1,2], Meireles, N[2]; Nicolau, P[2]; Carvalho, F[2]; Adour, C[1]; Casamali, C[1]; Delgado, J[1]; Thuler, LCS[3]; Bergmann, A[2]; Pinto LFR[1,4]

[1]Endoscopy Unit - Hospital do Cancer I/INCA; [2]Molecular Carcinogenesis Program – CPq/INCA ; [3]Clinical Research Division – CPq/INCA; [4]Biochemistry Department – IBRAG/UERJ

INTRODUCTION

- Pancreatic cancer (CP) is a very lethal tumor. It is the main cause of mortality among North-Americans[1], and the second among Brazilians[2], when considering the population from 40 to 79 years-old;
- Adenocarcinoma (ACP) is the prevalent histological type. It is frequently diagnosed at advanced stages[3], and therefore more often treated with non-curative intent[5];
- Prognosis may be negatively impacted by biological, clinical, and pathological factors, among others[4], resulting in an overall 5-year survival rate of 7.7%[1]. Nevertheless, some patients have a longer survival due to unknown features;
- Information about clinical, epidemiological and molecular characteristics of CP in Brazil is scarce.

OBJECTIVE



To evaluate the sociodemographic and clinical-pathological characteristics of CP/ACP in Brazil and at INCA, investigating their association with tumor molecular profiling and prognostic factors in a subgroup of the ACP patients.

METHODOLOGY

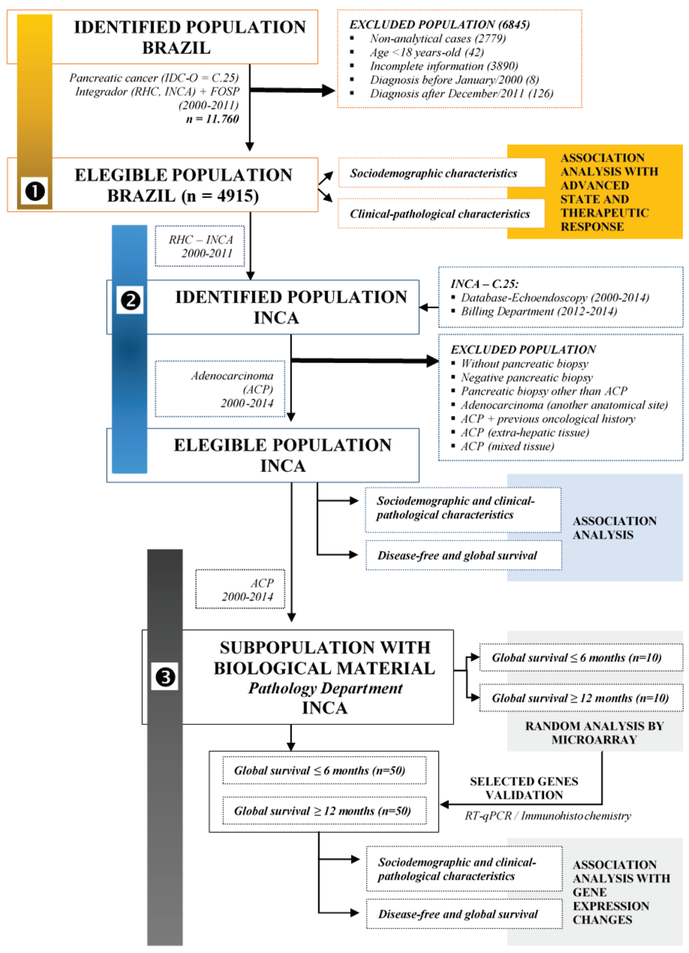


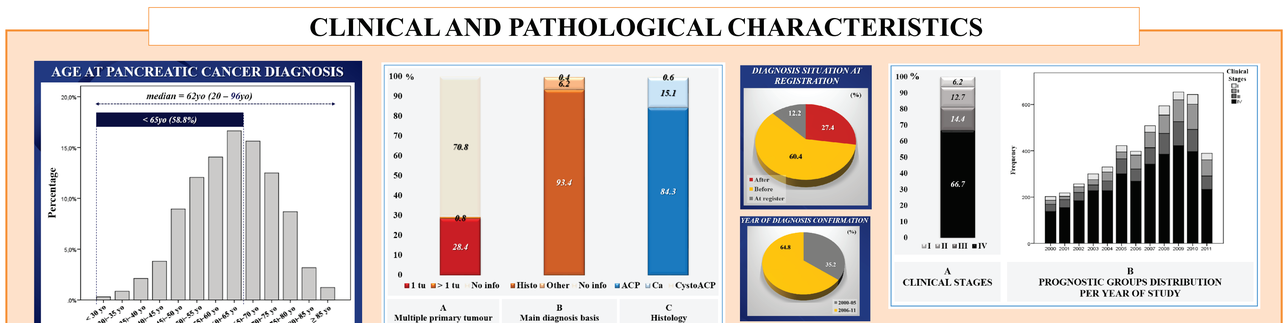
Figure – Study and population design: the Brazil (1) and INCA (2 and 3) steps are demonstrated with respective sources and populations.

CONCLUSION

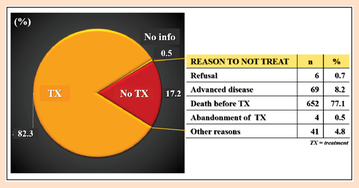
- Though it was observed some sociodemographic peculiarities (age < 65yo, white skin colour, and no alcoholic/tobacco habit), Brazilian CP patients generally get to hospital without previous diagnosis, that is often for ACP in an advanced disease stage, and are treated with CTX, usually in the Southeast region;
- Almost 50% of patients who received treatment had inadequate therapeutic response due to histological type (ACP), no diagnosis at hospital registration, advanced disease stage and others; Furthermore, almost 20% of patients died before treatment started, usually because of advanced stage disease;
- Future perspectives are to analyze data from INCA's patients and to associate their epidemiological data with wide genome analyzes of global gene expression by DNA microarray in ACP samples.

RESULTS

CLINICAL AND PATHOLOGICAL CHARACTERISTICS



TREATMENT



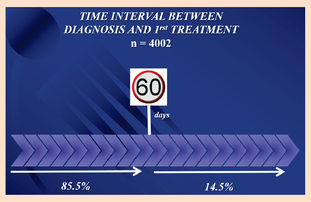
REASON TO NOT TREAT	n	%
Refusal	6	0.7
Advanced disease	69	8.2
Death before TX	652	77.1
Abandonment of TX	4	0.5
Other reasons	41	4.8

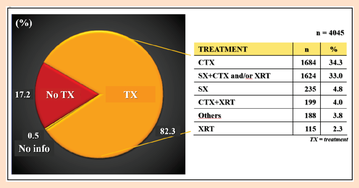
TX = treatment

TABLE 1 – ONCOLOGICAL TREATMENT STATUS ACCORDING TO CLINICAL STAGE OF THE 4891 PANCREATIC CANCER CASES

TREATMENT	CLINICAL STAGE – n (%)				TOTAL
	I	II	III	IV	
No TX	21 (6.8)	38 (6.1)	54 (7.6)	733 (22.5)	846 (17.3)
SX	46 (15.0)	42 (6.7)	36 (5.1)	111 (3.4)	235 (4.8)
SX+CTX and/or XRT	**175 (57.0)**	**397 (63.5)**	**286 (40.5)**	766 (23.6)	1624 (33.2)
XRT	6 (2.0)	16 (2.6)	37 (5.2)	56 (1.7)	115 (2.4)
XRT+CTX	5 (1.6)	21 (3.4)	56 (7.9)	117 (3.6)	199 (4.1)
CTX	28 (9.1)	92 (14.7)	216 (30.6)	**1348 (41.5)**	**1684 (34.4)**
Others	26 (8.5)	19 (3.0)	22 (3.1)	121 (3.7)	188 (3.8)
TOTAL	307 (100.0)	625 (100.0)	707 (100.0)	3252 (100.0)	4891 (100.0)

Legend: TX (treatment), SX (surgery), CTX (chemotherapy), XRT (radiotherapy). Obs.: 24 cases with no information were excluded / in bold the higher frequency values





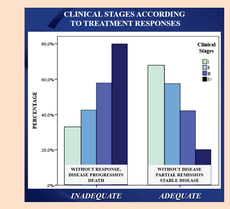
TREATMENT	n	%
CTX	1684	34.3
SX+CTX and/or XRT	1624	33.0
SX	235	4.8
CTX+XRT	199	4.0
Others	188	3.8
XRT	115	2.3

n = 4045
TX = treatment

TABLE 2 – DISEASE STATUS AT THE END OF 1st TREATMENT ACCORDING TO CLINICAL STAGE OF THE 3474 PANCREATIC CANCER CASES

DISEASE STATUS	CLINICAL STAGE – n (%)				TOTAL
	I	II	III	IV	
No disease	66 (27.4%)	98 (19.0%)	41 (7.3 %)	22 (1.0%)	227 (6.5%)
Partial remission	18 (7.5%)	39 (7.6%)	43 (7.7%)	76 (3.5%)	176 (5.1%)
Stable disease	**79 (32.8%)**	**159 (30.9%)**	153 (27.2%)	335 (15.5%)	726 (20.9%)
Disease in progression	14 (5.8%)	55 (10.7%)	96 (17.1%)	407 (18.9%)	572 (16.5%)
Clinical support	0 (0.0 %)	5 (1.0%)	7 (1.2%)	39 (1.8%)	51 (1.5%)
Death	64 (26.6%)	**159 (30.9%)**	**222 (39.5%)**	**1277 (59.2%)**	**1722 (49.2%)**
TOTAL	241 (100.0)	515 (100.0)	562 (100.0)	2156 (100.0)	3474 (100.0)

Obs.: Cases without informations or treatment were excluded / in bold the higher frequency values.



SOCIODEMOGRAPHIC CHARACTERISTICS

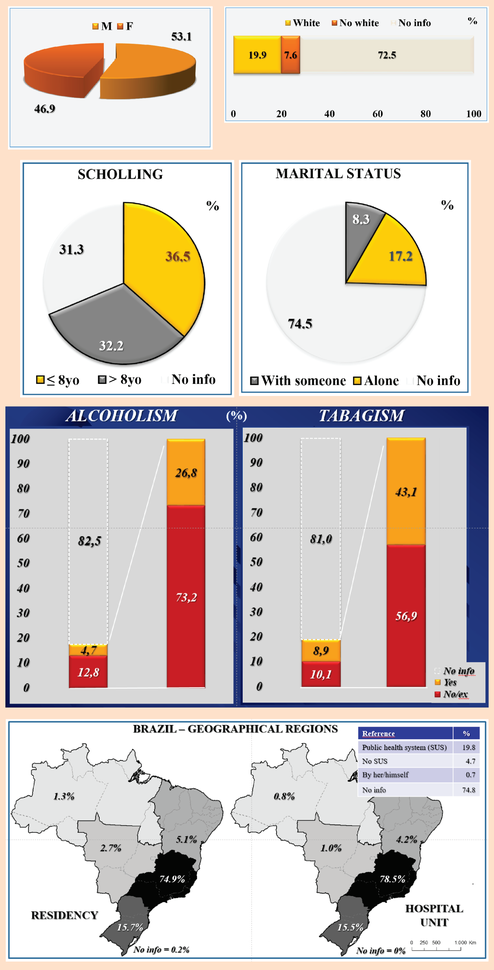


TABLE 6 – FREQUENCY OF THERAPEUTIC RESPONSE ACCORDING TO CLINICAL STAGE AND TREATMENT

CLINICAL STAGE	FIRST TREATMENT*	n	THERAPEUTIC RESPONSE n (%)*		*p* value ****
			ADEQUATE**	INADEQUATE***	
STAGE I	SX	43	26 (60.5)	17 (39.5)	0.606
	SX+CTX/XRT	145	102 (70.3)	43 (29.7)	
	XRT	6	5 (83.3)	1 (16.7)	
	CTX+XRT	5	3 (60.0)	2 (40.0)	
	CTX	18	10 (55.6)	8 (44.4)	
	Others	24	17 (70.8)	7 (29.2)	
	Total	241	163 (67.6)	78 (32.4)	
STAGE II	SX	36	18 (50.0)	18 (50.0)	0.167
	SX+CTX/XRT	359	219 (61.0)	140 (39.0)	
	XRT	14	8 (57.1)	6 (42.9)	
	CTX+XRT	17	9 (52.9)	8 (47.1)	
	CTX	72	32 (44.4)	40 (55.6)	
	Others	17	10 (58.8)	7 (41.2)	
	Total	515	296 (57.5)	219 (42.5)	
STAGE III	SX	29	12 (41.4)	17 (58.6)	***0.022***
	SX+CTX/XRT	253	117 (46.2)	136 (53.8)	
	XRT	32	20 (62.5)	12 (37.5)	
	CTX+XRT	51	20 (39.2)	31 (60.8)	
	CTX	176	63 (35.8)	113 (64.2)	
	Others	21	5 (23.8)	16 (76.2)	
	Total	562	237 (42.2)	325 (57.8)	
STAGE IV	SX	86	14 (16.3)	72 (83.7)	***0.047***
	SX+CTX/XRT	691	164 (23.7)	527 (76.3)	
	XRT	45	5 (11.1)	40 (88.9)	
	CTX+XRT	105	22 (21.0)	83 (79.0)	
	CTX	1116	204 (18.3)	912 (81.7)	
	Others	111	24 (21.6)	87 (78.4)	
	Total	2154	433 (20.1)	1721 (79.9)	
Totals#	SX	194	70 (36.0)	124 (64.0)	***<0.001***
	SX+CTX/XRT	1448	602 (41.6)	846 (58.4)	
	XRT	97	38 (39.2)	59 (60.8)	
	CTX+XRT	178	54 (30.3)	124 (69.7)	
	CTX	1382	309 (22.4)	1073 (77.6)	
	Others	173	56 (32.4)	117 (67.6)	
	Total	3472	1129 (32.5)	2343 (67.5)	

*Legend: * Excluded cases with no treatment information; * SX (surgery); CTX (chemotherapy); XRT (radiotherapy); ** Adequate response: partial remission, stable disease, and complete response; *** Inadequate response: disease progression, relapse or death; **** p <0.05 (Pearson test) = statiscally significant (bold)*

TABLE 5 – FREQUENCY OF THERAPEUTIC RESPONSE ACCORDING TO CLINICAL-EPIDEMIOLOGICAL VARIABLES

VARIABLES		THERAPEUTIC RESPONSE n (%)*		*p* value
		INADEQUATE (n = 2341*)	ADEQUATE (n = 1126)	
Gender	**Male**	1292 (55.1%)	571 (50.6%)	***0.012***
	Female	1053 (44.9%)	558 (49.4%)	
Idade	< 65yo	1393 (59.4%)	701 (62.1%)	0.129
	≥ 65yo	952 (40.6%)	428 (37.9%)	
Brazil's region of residency**	**SE and S**	2145 (91.6%)	999 (88.7%)	***0.006***
	N, NE and CO	196 (8.4%)	127 (11.3%)	
Year of diagnosis	2000 to 2005	776 (33.1%)	365 (32.3%)	0.654
	2006 to 2011	1569 (66.9%)	764 (67.7%)	
Diagnosis at institution registration (No treatment)	With diagnosis	766 (32.7%)	323 (28.7%)	***0.017***
	Without diagnosis	1573 (67.3%)	802 (71.3%)	
Histopathological type***	**ACP + CystoACP**	2032 (86.7%)	917 (81.2%)	***<0.001***
	Carcinoma	313 (13.3%)	212 (18.8%)	
Diagnosis-Treatment time interval	< 60 days	1992 (86.1%)	953 (85.2%)	*0.507*
	≥ 60 days	322 (13.9%)	165 (14.8%)	
Clinical stage	I and II	297 (12.7%)	459 (40.7%	***<0.001***
	III and IV	2048 (87.3%)	670 (59.3%)	
Treatment#	SX	124 (5.3%)	70 (6.2%)	***< 0.001***
	SX+CTX/XRT	846 (36.1%)	602 (53.3%)	
	XRT	59 (2.5%)	38 (3.4%)	
	CTX+XRT	124 (5.3%)	54 (4.8%)	
	CTX	1073 (45.8%)	309 (27.4%)	
	Others	117 (5.0%)	56 (5.0%)	

*Legend: *The percentage differences correspond to categories with no information; **N (North); NE (Northeast); CO (Midwest); SE (Southeast); S (South); *** ACP (adenocarcinoma); CystoACP (cystadenocarcinoma); * SX (surgery); CTX (chemotherapy); XRT (radiotherapy) / in bold the higher frequency values.*

TABLE 3 – CLINICAL STAGE ASSOCIATION ANALYSIS TO SOCIODEMOGRAPHICAL AND CLINICAL VARIABLES

VARIABLES		CLINICAL STAGE – n (%)		*p* value
		III and IV (n = 3983*)	I and II (n = 932*)	
Gender	**Male**	2162 (54.3%)	450 (48.3%)	***0.001***
	Female	1821 (45.7%)	482 (51.7%)	
Age	< 65yo	2362 (59.3%)	528 (56.7%)	0.139
	≥ 65yo	1621 (40.7%)	404 (43.3%)	
Brazil's region of residency **	N, NE and CO	373 (9.4%)	76 (8.2%)	0.248
	SE and S	3601 (90.6%)	854 (91.8%)	
Year of diagnosis	2000 to 2005	1465 (36.8%)	264 (28.3%)	***<0.001***
	2006 to 2011	2518 (63.2%)	668 (71.7%)	
Diagnosis at institution registration	With diagnosis	1381 (34.9%)	190 (20.5%)	***<0.001***
	Without diagnosis	2580 (65.1%)	737 (79.5%)	
Histopathological type***	**ACP + CystoACP**	3482 (87.4%)	690 (74.0%)	***<0.001***
	Carcinoma	501 (12.6%)	242 (26.0%)	

*Legend: * The totals are smaller than the elegible cohort: 4904 (Brazil's region of residency) and 4888 (Diagnosis at institution register), ** N (North); NE (Northeast); CO (Midwest); SE (Southeast); S (South), *** ACP (adenocarcinoma); CystoACP (cystadenocarcinoma) / in bold the higher frequency values.*

TABLE 4 – ASSOCIATED FACTORS TO ADVANCED CLINICAL STAGE (III AND IV)

VARIABLES		NOT ADJUSTED MODEL		ADJUSTED MODEL	
		OR* (CI**)	*p* value	OR (CI)	*p* value
Gender	Female	Reference	***<0.001***	Reference	***<0.001***
	Male	1.27 (1.10 – 1.47)		1.29 (1.11 – 1.49)	
Age	≥ 65yo	Reference	0.139	-	-
	< 65yo	1.11 (0.96 – 1.29)			
Brazil's region of residency	SE and S***	Reference	0.248	-	-
	N, NE and CO***	1.16 (0.90 – 1.51)			
Year of diagnosis	2000 to 2005	Reference	***<0.001***	Reference	***<0.001***
	2006 to 2011	1.47 (1.26 – 1.72)		1.49 (1.27 – 1.74)	
Diagnosis at institution registration (No treatment)	With diagnosis	Reference	***<0.001***	Reference	***<0.001***
	Without diagnosis	2.08 (1.75 – 2.47)		2.11 (1.78 – 2.52)	
Histopathological type	Carcinoma	Reference	***<0.001***	Reference	***<0.001***
	ACP# or CistoACP#	2.44 (2.05 – 2.90)		2.35 (1.97 – 2.81)	

*Legend: * Odds ratio; ** Confiance interval, *** N (North); NE (Northeast); CO (Midwest); SE (Southeast); S (South); * ACP (adenocarcinoma); CystoACP (cystadenocarcinoma) / in bold the higher frequency values.*

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