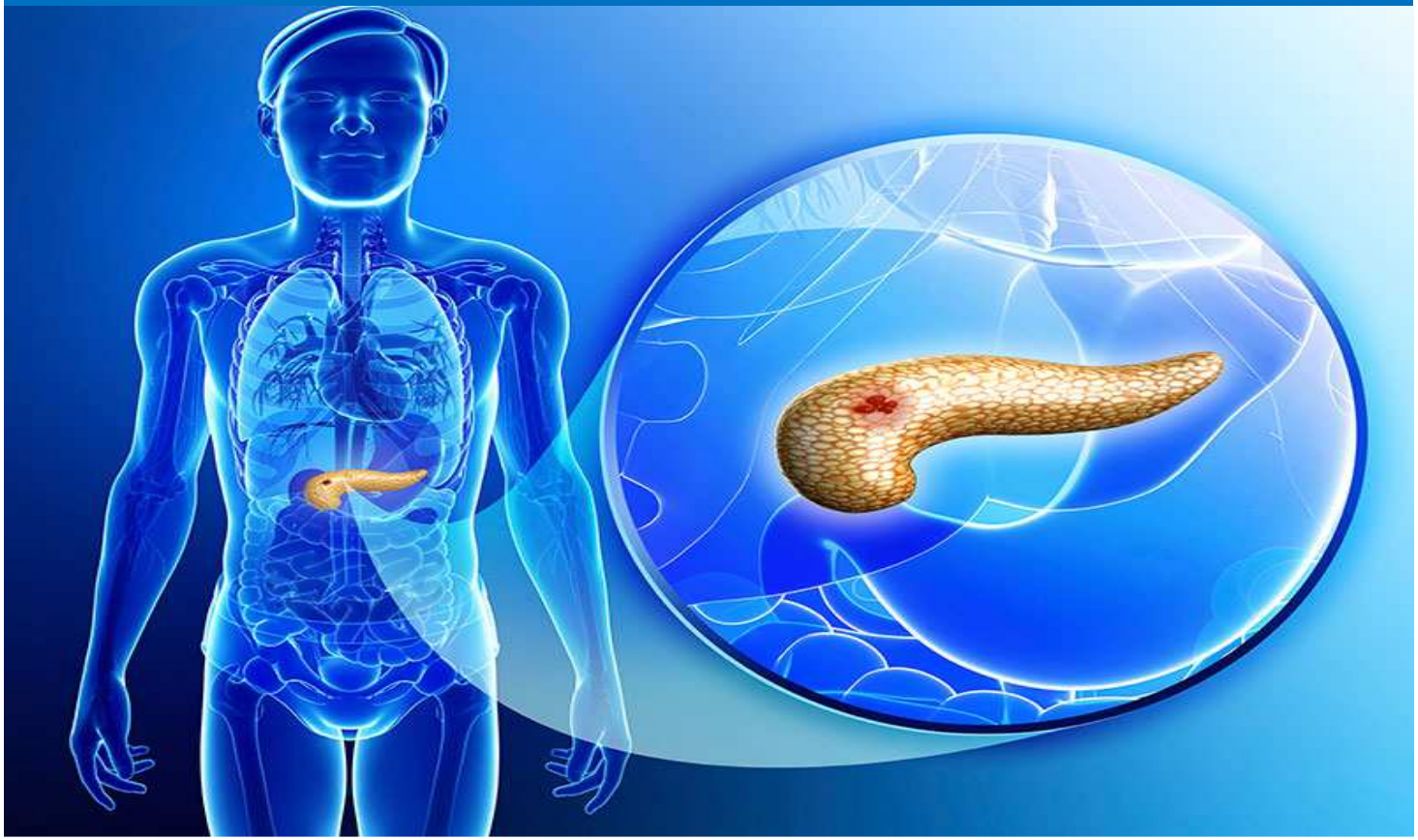
13-15 Aprile 2016
Reggio Children c/o Centro Internazionale Loris Malaguzzi – REGGIO EMILIA

Gestione e prognosi dei pazienti con adenocarcinoma pancreatico: dati del Registro ad alta risoluzione della provincia di Reggio Emilia



Cassetti Tiziana
SC di Gastroenterologia ed endoscopia digestiva
Arcispedale Santa Maria Nuova, IRCCS
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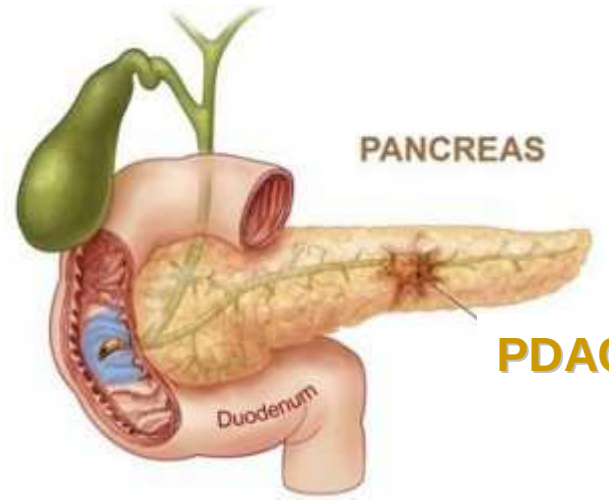
Sant Milena
Minicozzi Pamela
Vicentini Massimo
Sacchettini Claudio
Mancuso Pamela
Bonfarnuzzo Simone
Ballotari Paola
Mangone Lucia
Giorgi Rossi Paolo
Sassatelli Romano

Obiettivi:



- ✓ Valutare il management dei pazienti con ADK del pancreas e il suo effetto sul rischio di morte
- ✓ Identificare i fattori prognostici

MATERIALI E METODI

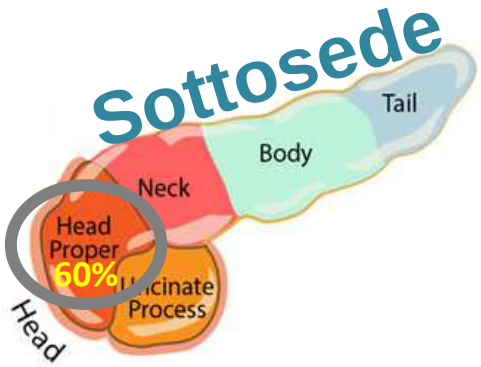
- ☒ Dati incidenti 2008-2012
- ☒ Sesso, età, sottosede, morfologia (NOS / ADK), stadio (I, II, III, IV, X)
- ☒ Esclusione dei DCO e dei NET
- ☒ Lo stato in vita aggiornato al 31/12/2015

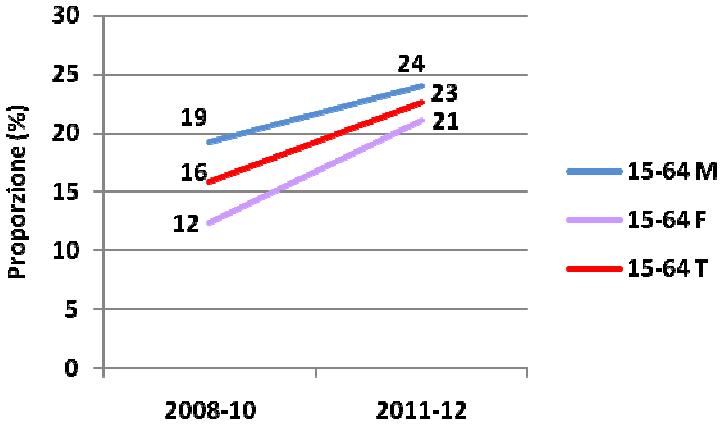
- ☒ trattamenti combinati:
  - ✓ chirurgia resettiva/palliativa
  - ✓ chemio/radioterapia +/- trattamento chirurgico
  - ✓ nessuna terapia
- ☒ Sopravvivenza relativa a 3 anni
- ☒ Eccesso di rischio di morte (RERs) modelli multivariati (età, stadio, trattamento e periodo di diagnosi)

- ☒ HR è stato calcolato utilizzando il **modello di Cox** aggiustato per:
  - ✓ età (≤54, 55-74, 75-84, 85+)
  - ✓ residenza (area urbana, sub-urbana e montana)
  - ✓ Ca19.9 (≤ e >100 aggiustato per ittero)
  - ✓ diabete diagnosticato prima del PDAC (si/no) [link con il Registro diabete di RE]
- ☒ Misura della concordanza fra EUS e TAC sull'identificazione degli N+ [**Kappa di Cohen (κ)**]

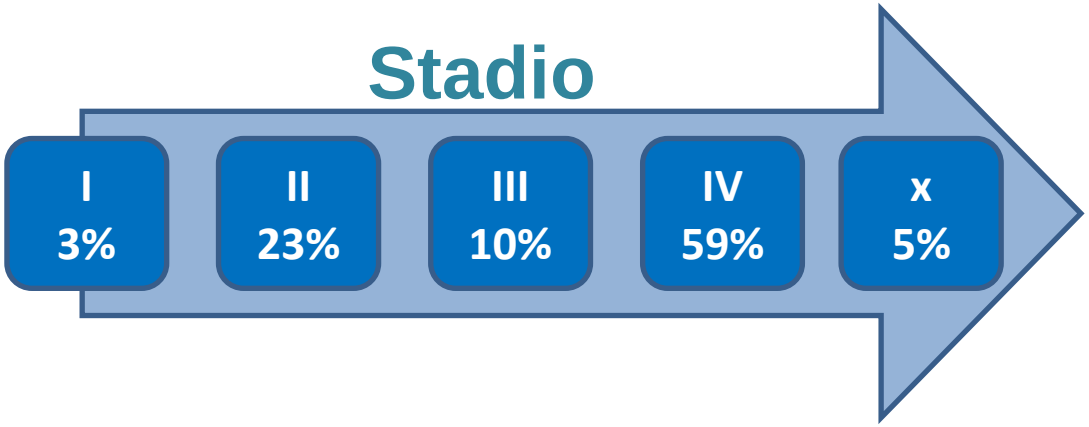
RISULTATI Obiettivo 1

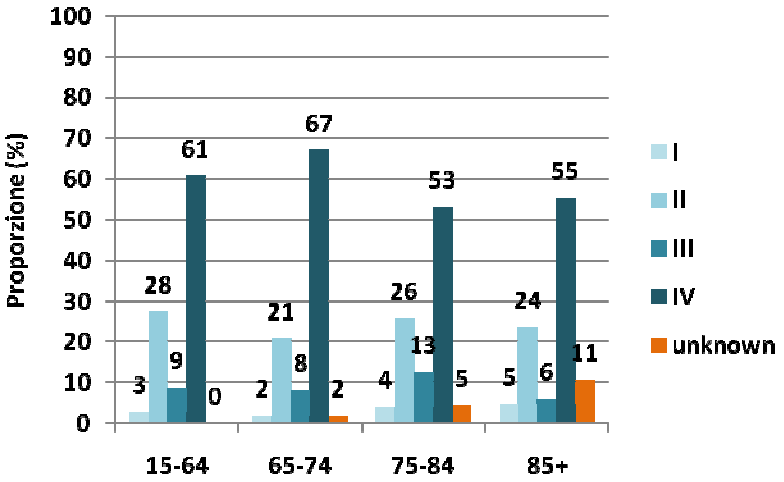
550 pazienti





52% età >75 anni
aumentano le diagnosi nei giovani
(15-64 anni; 16% vs 23% p=0.04)





RISULTATI Obiettivo 1

Chirurgia Resettiva: ≈ 14%

Chirurgia Palliativa: ⇩ 64% vs 36%, p=0.112

Nessun Trattamento: 50%

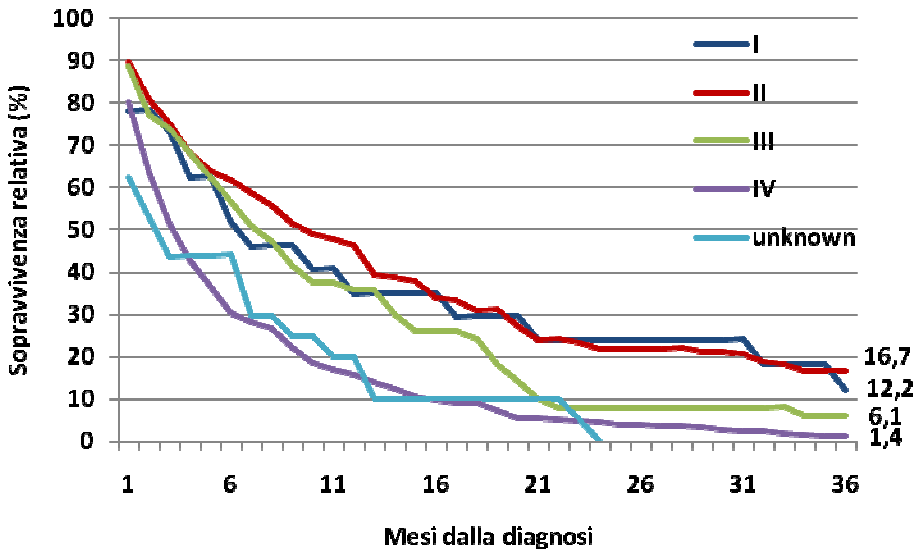
- ✓ Anziani
- ✓ Stadio avanzato
- ✓ Comorbidità

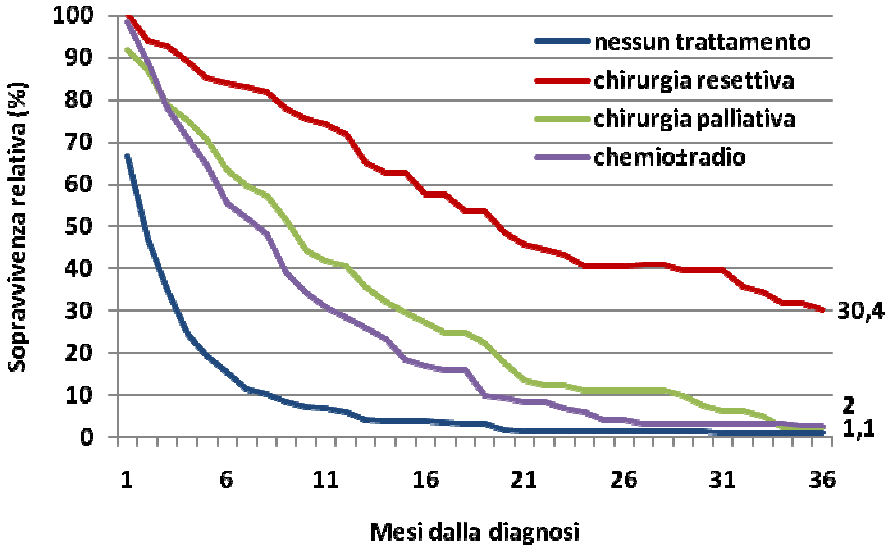
3-year overall (OS) and relative (RS) survival (NOT age-adjusted)

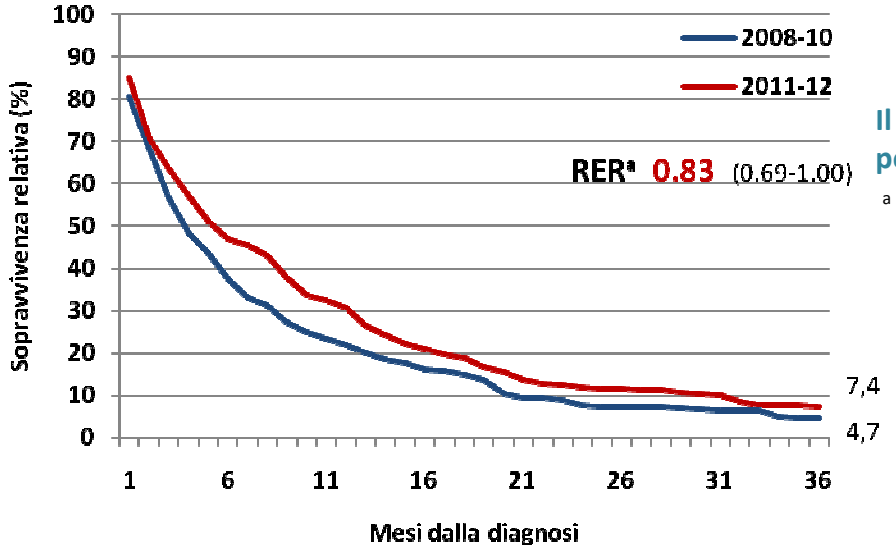
	OS	95%CI	RS	95%CI
Curative surg_yes	28.6	19-38.9	30.4	20.2-41.4
Curative surg_no	1.5	0.7-3	1.7	0.8-3.4
Nessun trattamento	0.8	0.2-2.6	1.1	0.2-3.8
Chir res +/- CT/RT	28.6	19-38.9	30.4	20.2-41.4
Chir pal +/- CT/RT	2.4	0.5-7.6	2.5	0.5-8.0
CT /RT	2.5	0.7-6.5	2.6	0.7-6.7

RISULTATI Obiettivo 1

Sopravvivenza







Il rischio di morte diminuiva nel periodo in studio (RER=0.8, p=0.03)

[a] aggiustato per età, stadio, trattamento e sesso

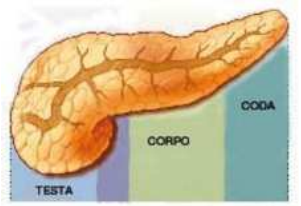
RISULTATI Obiettivo 2

	Haz. Ratio	Std. Err.	z	P>z	[95% Conf.	Interval]
Età (ref<55)						
55-74	1.49	0.27	2.13	0.033	1.03	2.1
75-84	2.24	0.42	4.23	0	1.54	3.26
85+	3.34	0.70	5.76	0	2.22	5.04

	Haz. Ratio	Std. Err.	z	P>z	[95% Conf.	Interval]
Sesso (ref M)						
F	0.85	0.07	-1.79	0.073	0.71	1.01

	Haz. Ratio	Std. Err.	z	P>z	[95% Conf.	Interval]
Periodo (ref 2008-10)	0.83	0.07	-2.07	0.04	0.69	0.99
2011-2012						

	Haz. Ratio	Std. Err.	z	P>z	[95% Conf.	Interval]
Sottosede (ref testa)						
Corpo	1.05	0.17	0.29	0.77	0.77	1.43
coda	0.99	0.15	0.04	0.97	0.74	1.33
non noto	1.16	0.15	1.18	0.24	0.90	1.50
stadio (ref I)						
II_III	0.92	0.24	0.31	0.76	0.54	1.56
IV	1.96	0.52	2.52	0.012	1.16	3.29
non noto	1.31	0.46	0.79	0.431	0.66	2.60



OncoTargets and Therapy

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ORIGINAL RESEARCH

Impact of diabetes mellitus on the survival of pancreatic cancer: a meta-analysis

This article was published in the following Dove Press journal:
OncoTargets and Therapy
22 March 2016
Number of times this article has been viewed

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Background: Diabetes mellitus (DM) is a risk factor for pancreatic cancer (PC), but its prognostic value in PC is still unclear. To elucidate this issue, we systematically reviewed the evidence concerning the association between diabetes status and PC.

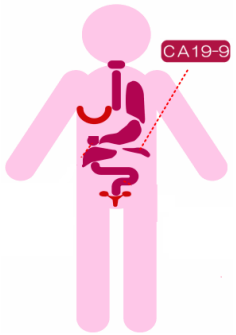
Methods: Medline and EMBASE databases were searched to identify the eligible studies. Overall and subgroup analyses were performed to detect the discrepancy of prognosis according to diabetes status. Hazard ratios (HRs) with 95% CI were used to estimate the effect size.

Results: Eighteen studies including 16,181 patients with sample size ranging from 113 to 4,658 were pooled in this meta-analysis. Results showed that patients with DM had worse survival (HR 1.19, 95% CI: 1.07–1.32). In view of the impact of diabetes duration and tumor stage on the outcomes, we classified the studies into different groups. The results indicated that DM was associated with survival in both long-standing diabetes (HR 1.26, 95% CI: 1.14–1.40) and recent-onset diabetes (HR 1.29, 95% CI: 1.09–1.51). Data regarding localized disease (HR 1.57, 95% CI: 1.00–2.46) and nonlocalized (locally advanced and metastatic) disease (HR 1.42, 95% CI: 1.16–1.73) verified that the prognostic value was independent of tumor stage.

Conclusion: Our results suggested that patients with DM were associated with worse survival than those without DM. Diabetes may be a predictive factor of survival in patients with PC. Surveillance of diabetes status and antidiabetes medication administration after the diagnosis of PC is of clinical importance.

Keywords: diabetes mellitus, pancreatic cancer, survival, meta-analysis

RISULTATI Obiettivo 2



	Haz. Ratio	Std. Err.	z	P>z	[95% Conf.	Interval]
Ca19.9 (ref >100)						
non noto	1.41	0.18	2.66	0.008	1.09	1.82
>200	1.12	0.15	0.85	0.39	0.86	1.45

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2015
Pancreatic Adenocarcinoma

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Discussion

Preoperative CA 19-9 levels correlate with both AJCC staging and resectability and thus can provide additional information for staging and determining resectability, along with information from imaging, laparoscopy, and biopsy.[166-168]

CA 19-9 also seems to have value as a prognostic and a predictive marker for pancreatic cancer in various settings. In resectable disease

treatment CA 19-9 levels were a good prognostic marker in patients receiving neoadjuvant therapy with or without subsequent resection.[175] This study found that a normalization of CA 19-9 to <40 U/mL was associated with improvements in OS in non-resected (15 months vs. 11 months; *P* = .02) and resected (38 months vs. 26 months; *P* = .02) patients.

In the advanced disease setting, data support the role of CA 19-9 as a

were
dition,

76-181

For example, a recent study that pooled individual patients' data from 6 prospective trials found that a decline in CA 19-9 levels from baseline to after surgery and 2 rounds of adjuvant therapy were associated with a better outcome.[169] In fact, increases of <5% in CA 19-9 were also associated with improved outcomes compared to patients with larger increases (OS, 10.3 months vs. 5.1 months; *P* = .002).

It is important to note that CA 19-9 may be undetectable in Lewis antigen-negative individuals.[182] Furthermore, CA 19-9 may be falsely positive in cases of biliary infection (cholangitis), inflammation, or biliary obstruction (regardless of etiology) and do not necessarily indicate cancer or advanced disease.[183,184] Preoperative measurement of CA 19-9 levels (category 3) is therefore best performed after biliary decompression is complete and bilirubin is normal. If biliary decompression is not performed in a jaundiced patient, CA 19-9 levels can be assessed (category 3), but they do not represent an accurate baseline.

In the neoadjuvant/borderline resectable setting, a recent study of 141 patients treated at MD Anderson Cancer Center found that post-

 MS-12

Indian J Surg Oncol (April–June 2011) 2(2):88–100
DOI 10.1007/s13193-011-0042-1

REVIEW ARTICLE

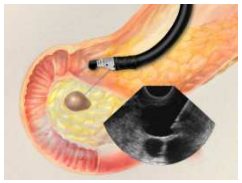
Serum CA 19-9 as a Biomarker for Pancreatic Cancer—A Comprehensive Review

Umashankar K. Ballehaninna · Ronald S. Chamberlain

increased false positivity in the presence of obstructive jaundice (10–60%)

- ✓ **A CA 19-9 serum:**
  - ✓ **level of <100 U/ml implies likely resectable disease**
  - ✓ **levels >100 U/ml may suggest unresectablity or metastatic disease.**

RISULTATI Obiettivo 2



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```
Logistic regression                               Number of obs   =        573
                                                  LR chi2(8)      =     140.99
                                                  Prob > chi2     =     0.0000
Log likelihood = -326.65806                       Pseudo R2       =     0.1775

------------------------------------------------------------------------------
     eus_new | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
Età ≤54
       55-74|   .9154011   .3385447    -0.24   0.811
       75-84|   .7397232   .2785692    -0.80   0.423
        _≥85|   .1402696   .0637125    -4.32   0.000
     _ISex_2 |   .5508909   .1076902    -3.05   0.002
Periodo 1vs2 |   2.417858   .4683381     4.56   0.000
Stadio II-III|   2.258508    1.16815     1.58   0.115
          IV |   .4001082   .2018933    -1.82   0.069
    Non noto |   .5343054   .3619784    -0.93   0.355
       _cons |    1.78666   1.110494     0.93   0.350
------------------------------------------------------------------------------
```

sesso 1 m 2 f
periodo 1=2008-2010 2=2011-2012

All'aumentare dell'età e dello stadio alla diagnosi le EUS eseguite diminuiscono

Uso di EUS ed EUS-FNA

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Pancreatic Adenocarcinoma

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CLINICAL PRESENTATION | WORKUP

Clinical suspicion of pancreatic cancer or evidence of dilated pancreatic and/or bile duct (stricture) → Pancreatic protocol CT (See PANC-A)

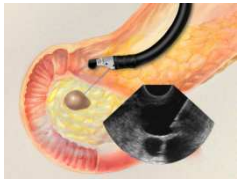
Mass in pancreas on imaging:
- No metastatic disease → • Multidisciplinary review[a] • Consider endoscopic ultrasonography (EUS)[b] • Liver function tests • Chest imaging → Surgical candidate (See PANC-2)
- Metastatic disease → Biopsy confirmation of metastatic site → See Metastatic Disease (PANC-9)

No mass in pancreas on imaging:
- No metastatic disease → • Liver function tests • Chest imaging • EUS[b] (preferred) • MRI/magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP) as clinically indicated → If studies are consistent with pancreatic cancer, surgical consultation is recommended (See PANC-2)
- Metastatic disease → • Biopsy confirmation of metastatic site • EUS[b] → See Metastatic Disease (PANC-9)

[a]Multidisciplinary review should ideally involve expertise from diagnostic imaging, interventional endoscopy, medical oncology, radiation oncology, surgery, and pathology.
[b]EUS-FNA if clinically indicated.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

RISULTATI Obiettivo 2



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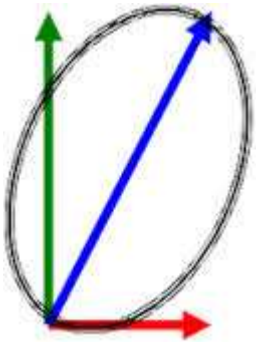
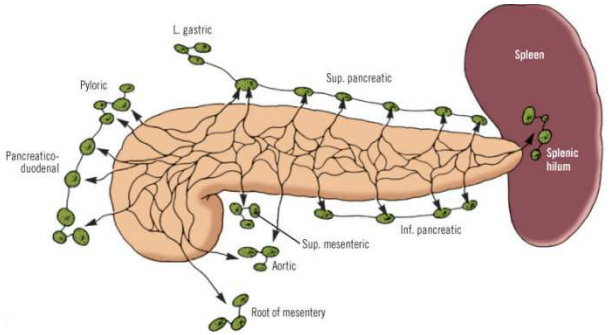
```
Paired t test
------------------------------------------------------------------------------
Variable |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
tc_dia~o |     139     33.1223    1.410392    16.62827    30.33353    35.91107
eus_di~o |     139    33.96403    1.079202     12.7236    31.83012    36.09794
---------+--------------------------------------------------------------------
    diff |     139   -.8417266     1.37804    16.24685    -3.56653    1.883077
------------------------------------------------------------------------------
     mean(diff) = mean(tc_diametro - eus_diametro)                 t =  -0.6108
 Ho: mean(diff) = 0                              degrees of freedom =      138

 Ha: mean(diff) < 0           Ha: mean(diff) != 0           Ha: mean(diff) > 0
 Pr(T < t) = 0.2712         Pr(|T| > |t|) = 0.5423          Pr(T > t) = 0.7288
```



- ✓ **Diametro della lesione TAC vs EUS: non c'è differenza**
- ✓ **Nel periodo 2011-2012 aumentano in proporzione sia l'EUS che EUS-FNA mentre la TAC rimane pressocchè costante.**

RISULTATI Obiettivo 2




```
. tab eus_meta_r tc_meta_r if stadio!=3, miss
```

eus_meta_r	tc_meta_r: Assente	Unica	Multipla	Missing	Total
Assente	43	2	15	19	79
Unica	2	0	2	1	5
Multipla	13	0	44	12	69
Missing	34	0	39	28	101
Total	92	2	100	60	254

Nel 26% dei casi l'EUS individua metastasi linfonodali quando nella TAC sono assenti; quindi cambia l'cN nella stadiazione

```
. kap tc_meta eus_meta if (tc_meta!=. & eus_meta!=. & stadio!=3)
```

Agreement	Expected Agreement	Kappa	Std. Err.	Z	Prob>Z
71.90%	47.57%	0.4640	0.0847	5.48	0.0000

TAC ed EUS per la determinazione delle metastasi linfonodali presentano una concordanza moderata (κ=0.46)

CONCLUSIONI

- ✓ L'aumento dei pazienti di giovane età
- ✓ Nessun miglioramento nello stadio alla diagnosi
- ✓ Aumento della sopravvivenza nel periodo 2011-2012 deve essere ancora oggetto di ricerca.

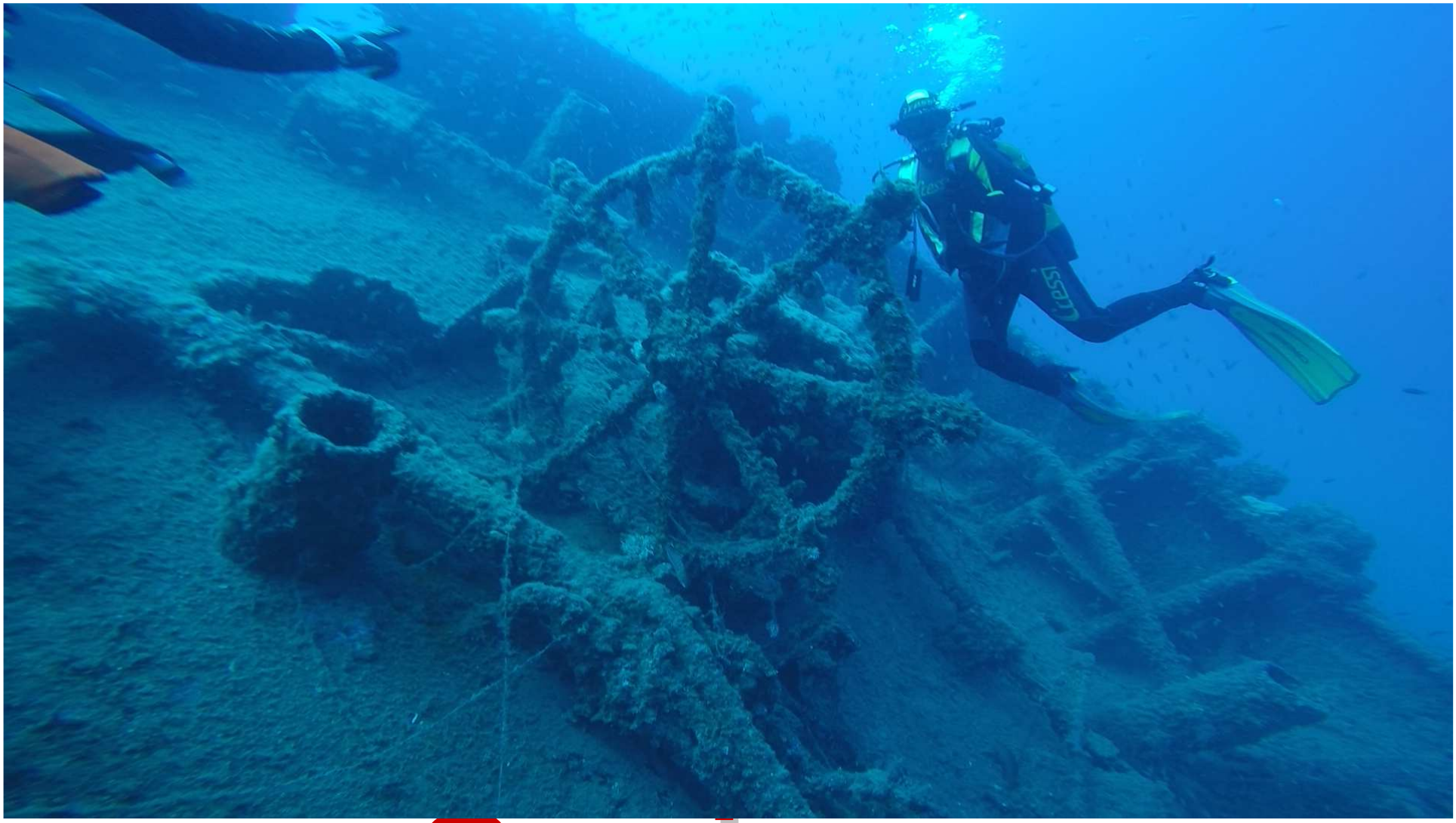
- ✓ Età, stadio IV, sesso sono i principali fattori prognostici
- ✓ Lo stato di diabetico è fortemente predittivo di una bassa sopravvivenza
- ✓ In caso di M0, l'EUS diventa uno strumento più accurato della TAC nella definizione dell'N modificando la stadiazione e l'approccio terapeutico.

Bisogna avere il coraggio di lanciarsi verso nuove scoperte

Il Geografo

- *È una persona anziana, un burocrate, uno studioso che trascrive in grossi libri le informazioni degli esploratori che incontra.*
- *Conosce la geografia di tutti gli altri pianeti, ma non sa nulla del suo, in quanto non lo ha mai esplorato.*
- *Si preoccupa di documentare quanto riferitogli dagli altri, ma rifiuta di fare uno sforzo di esperienza e conoscenza diretta rendendo così sterile la sua attività.*

- *Ha bisogno del racconto degli altri per conoscere le cose mentre per il Piccolo Principe è importante sforzarsi di conoscere le cose da soli.*



Grazie per l'attenzione

PANCREATIC CANCER EUROPE
The European Multi-Stakeholder Platform on Pancreatic Cancer

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Pancreatic Cancer Declaration

By 2020, pancreatic cancer is set to be the 2nd leading cause of death by cancer, if no action is taken[1]. This Declaration by the European Multi-Stakeholder Platform on Pancreatic Cancer outlines what action is needed to halt this violent and deadly disease.

By 2020: 5 key targets

1. Aumentare la consapevolezza

2. Colmare le lacune nelle politiche di controllo

3. Migliorare la diagnosi

4. Implementare la raccolta di dati efficienti e i registri tumori del pancreas

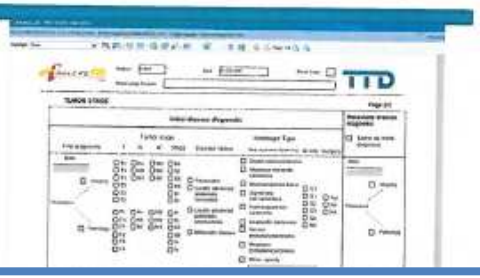
5. Investire nella ricerca

PancreOS:
European Registry of Pancreatic Cancer

PancreOs is a hospital-based clinical cancer registry that will include newly diagnosed pancreatic cancer patients and information on the clinical aspects of the disease, covering the initial symptoms, the diagnostic procedures and the treatments applied.

Variables:

- Personal details and socio-demographic variables
- Medical history
- Lifestyle factors



EurocanPlatform

WP11 Clinical Epidemiology

A comparison of patient population, surgical resection, adjuvant treatment, and outcome among patients with pancreatic cancer – a study among EurocanPlatform members (Lei Huang, Masoud Babaei, Lina Jansen, Yesilda Balavarca, Petra Schrotz-King, Hermann Brenner)

current treatment and diagnostic strategies. It will be the first initiative of this kind in Europe.

Stage 2- Registry in Europe

Grazie per l’attenzione