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ARTICLE

DaPeCa-9 – cohabitation and socio-economic conditions predict penile cancer-specific survival in a national clinical study from Denmark

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ABSTRACT

Background: Cohabitation and social conditions predict prognosis in several cancers; recent data suggest this might also be the case in penile cancer.

Objective: To assess the prognostic significance of cohabitation, living arrangements and socio-economic conditions for cancer-specific survival (CSS) in patients with penile squamous cell carcinoma (pSCC)

Methods: We retrospectively evaluated CSS in 429 pSCC patients from a 10-year period. We assessed cohabitation, living arrangements and socio-economic conditions(SEC) as prognostic predictors. Kaplan–Meier estimates and Cox hazard rates (HR) with 95% confidence intervals were used for analysis.

Results: Out of 429 pSCC patients, 137 (32%) were living alone and 292 (68%) were cohabiting. With a Cox HR at 1.91 (95% CI 1.3–2.98) patients living alone had a significantly lower median five-year survival rate at 69% (95% CI 60-77%) compared to cohabiting patients at 83% (95% CI 78–87%), $p = 0.002$. Comparing 60 (14%) from higher to 202 (47%) from medium and 95 (22%) patients from lower socio-economic groups we found Cox HRs at 1, 2.4 (95% CI 1.0-5.7, $p = 0.04$) and 3.4 (95% CI 1.4-8.1, $p < 0.01$) respectively. When comparing living arrangements, the trend that patients living in apartments and institutions had poorer outcomes than patients living in a house did not reach statistical significance.

Conclusions: Living alone and in poor socio-economic conditions predict poor prognosis in penile cancer in this national study. We make the case for further research in efforts to minimize cancer inequality pSCC patients.

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Penile cancer; penile squamous cell carcinoma (pSCC); socio-economic conditions (SEC); cancer-specific survival; cohabitation; living arrangements

Introduction

Penile cancer has an incidence of 0.5 – 2.1/100.000 men in Europe and North America. With higher incidence in parts of Africa and South America [1–3]. Numerous risk factors have been recognized including phimosis, human papilloma virus infection, and tobacco use [3, 4].

Few population-based studies have investigated the relation between living arrangements, social conditions, and risk of penile squamous cell carcinoma. Studies in breast, colorectal and bladder cancer have demonstrated cohabitation as an independent prognostic factor [5–7]. This has also been indicated in previous studies on penile cancer [8–10], though findings are not equivocal.

This study aims to investigate the prognostic importance of cohabitation, living arrangements and socio-economic conditions in a large nationwide retrospective Danish cohort of men with invasive pSCC.

Methods

We assessed 429 patients diagnosed with pSCC from a National Danish retrospective penile cancer cohort over a 10-year period. Data on the predictive value of elevated body mass index have previously been published on this cohort [11]. The cohort database was established by chart review at the only five Danish university hospitals treating penile cancer during the period. Patients not referred to university hospital departments due to age, comorbidity or death before referral were excluded. The parameters retrieved for this study included date of birth, date of diagnosis, pathological tumour information, smoking status, living arrangements, cohabitation and occupation at the time of diagnosis. Our dataset did not include information about changes in cohabitation status over time and hence all data refers to status at diagnosis. On the basis of occupation, or previous occupation in retired men, we categorized patients into five socio-economic groups according to the directions outlined by the Danish national authority on socio-economic conditions [SECs] 'socialforskningsinstituttet' [12].

For the analysis, we pre-defined three categories of higher (groups 1 and 2) medium (groups 3 and 4) and lower (group 5) socio-economic status. In 72 patients data on occupation was not available in the record.

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Clinical pathway milestones and clinical intervals

To assess possible differences in clinical trajectories between patients cohabiting and patients living alone, we analyzed clinical pathway milestones and clinical intervals. We defined patient interval as the period from reported first symptom to first visit to any medical practitioner for the symptoms caused by the disease later proven to be penile cancer. We defined treatment interval as the time between referral to treatment and start of definitive primary treatment, and we defined the total interval as the time from reported first symptom to start of definitive primary treatment.

Statistical analysis

Penile cancer-specific survival was estimated by the Kaplan–Meier method and the difference between groups was analysed by a Cox regression model adjusting for age as a continuous variable with 95% confidence intervals.

To test if the socio-economic group was an independent predictor of cancer-specific survival, we fitted a Cox regression model adjusting estimates for age and cohabiting status. Penile cancer-specific death was defined as death from penile carcinoma or death from complications due to treatment for penile carcinoma. Patients alive at the end of follow-up were censored at that date.

For statistical analysis, we used Stata Statistical Software: Release 13, TX: Statacorp. A p-value of 0.05 or less was considered statistically significant.

Study approval

This study received approval by the regional authorities and the Danish Data Protection Agency, file numbers 1-16-02-95-13 and 2007-41-0630 as well as from the Danish Health and Medicines Authority.

Results

Among 429 pSCC patients, 292 (68%) were cohabiting and 137 (32%) living alone. There was no difference in age ($p = 0.82$), AJCC stage ($p = 0.14$) and smoking status ($p = 0.35$) between patients living alone and cohabiting (Table 1).

Table 1. Patient characteristics.

Characteristic	Total n(%)	Living alone n (%)	Married/ cohabiting n (%)	p value
No.	429 (100)	137 (32)	292 (68)	
Age, years		66.33	66.14	0.82[a]
Smoking Status				
never	170 (40)	50 (36)	120 (41)	0.35[b]
current daily	216 (50)	77 (56)	139 (48)	
former	38 (9)	9 (7)	29 (10)	
unknown	5 (1)	1 (1)	4 (1)	
Socio-economic group				
Higher (1-2)	60 (14)	6 (4)	54 (18)	<0.0001[b]
Medium (3-4)	202 (47)	58 (42)	144 (49)	
Lower (5)	95 (22)	49 (36)	46 (16)	
No data	72 (17)	24 (18)	48 (17)	
Living Arrangements				
House	257 (60)	53 (39)	204 (70)	<0.0001[b]
Apartment	151 (35)	69 (50)	82 (28)	
Institution	21 (5)	15 (11)	6 (2)	
Tumor Stage				
1	237 (55)	62 (45)	175 (60)	0.001[c]
2	120 (28)	43 (31)	77 (26)	
3	61 (14)	24 (18)	37 (13)	
4	11 (3)	8 (6)	3 (1)	
American Joint Committee on Cancer 2010 (AJCC)-stage				
0	240 (56)	68 (50)	172 (59)	0.14[b]
1	72 (17)	27 (20)	45 (15)	
2	33 (8)	11 (8)	22 (8)	
3	26 (6)	6 (4)	20 (7)	
4	58 (13)	25 (18)	33 (11)	
Treatment				
Local resection	208 (49)	65 (48)	143 (49)	0.29[c]
Partial penectomy	159 (37)	44 (32)	115 (39)	
Total penectomy	62 (14)	28 (20)	34 (12)	

[a]Unpaired samples t-test; [b]Fisher's exact test; [c]Nonparametric test for trend.

Association between cohabitation and socio-economic group

Out of 60 patients from the higher socio-economic groups, 54 (90%) were cohabiting, whereas it was only 144 of 202 (71%) and 46 of 95 (48%) of patients from medium and lower socio-economic groups ($p < 0.0001$).

Association between cohabitation and living arrangements

Out of 257 patients living in a house, 204 (79%) were cohabiting, whereas it was only 82 of 151 (54%) of patients living in an apartment and 6 of 21 (29%) of patients living in an institution ($p < 0.0001$).

Cancer-specific death predicted by cohabitation

The age-adjusted Cox hazard rate for penile cancer-specific death was 1.9 (95% CI 1.3-2.9, $p = 0.002$) for patients living alone compared to cohabiting patients. The median five-year cancer-specific survival rate was 69% (95% CI 60–77%) for patients living alone compared to cohabiting patients at 83% (95% CI 78–87%), $p = 0.002$ (Table 2 and Figure 1).

Clinical intervals and cohabitation

The patient intervals of patients cohabiting and patients living alone were 120.8 (95% CI 103.2–138.5) days and 143.6 (95% CI 103.6–183.6) days, $p = 0.23$. The treatment intervals of patients cohabiting and patients living alone were 17.8 (95% CI 14.7–21.0) days and 19.9 (95% CI 16.5–23.4) days, $p = 0.43$. The total intervals of patients cohabiting and patients living alone were 223.5 (95% CI 201.3–245.7) days and 257.0 (95% CI 205.5–308.5) days, $p = 0.17$.

Cancer-specific death predicted by socio-economic group

The age-adjusted Cox hazard for penile cancer-specific death was 2.43 (95% CI 1.04–5.72, $p = 0.04$) in medium and 3.35

(95% CI 1.38–8.12, $p = 0.007$) in lower socio-economic groups with higher socio-economic groups as normalized comparator. The age- and cohabiting status-adjusted Cox hazard for penile cancer-specific death was 2.19 (95% CI 0.9–5.2, $p = 0.07$) in medium and 2.7 (95% CI 1.1–6.6, $p = 0.03$) in lower socio-economic groups again with higher socio-economic groups as normalized comparator.

Table 2. Predicting penile cancer specific survival by socio-economic conditions.

Characteristic	Patients *n*(%)	Cox hazard ratio (95 % CI)	*p*-value
No.	429 (100)		
Cohabiting status			
Married, cohabiting	292 (68)	1	
Living alone	137 (32)	1.90 (1.3–2.9)	0.002[a]
		1	
Socio-economic group			
Higher (1–2)	60 (14)	1	
Medium (3–4)	202 (47)	2.43 (1.04–5.72)	0.04[a]
Lower (5)	95 (22)	3.35 (1.38–8.12)	0.007[a]
No data	72 (17)	1.99 (0.74–5.34)	0.17[a]
Living arrangements			
House	257 (60)	1	
Appartment	151 (35)	1.50 (0.98–2.32)	0.06[a]
Institution	21 (5)	1.90 (0.81–4.65)	0.14[a]
Current smoker			
No	213 (50)	1	
Yes	216 (50)	1.90 (1.23–2.91)	0.004[a]

CI = confidence interval; [a]Cox regression model adjusted for age.

Predictive value of living arrangements

When comparing cancer-specific survival among patients with different living arrangements, we found no significant differences between patients living in a house, patients living in apartments (Cox hazard rate 1.5 (95% CI 0.98–2.32, $p = 0.06$)) and patients living in institution (Cox hazard rate 1.9 (0.81–4.65, $p = 0.14$), see Table 2 and Figure 1).

Smoking status and survival

Out of 429 patients, 216 (50%) were current smokers. The age-adjusted Cox hazard rate for penile cancer-specific death was 1.9 (95% CI 1.23–2.91, $p = 0.004$) for current smokers compared to patients who were not current smokers.

Discussion

In the current study, we found cohabitation to be of prognostic significance in penile cancer. We also found a

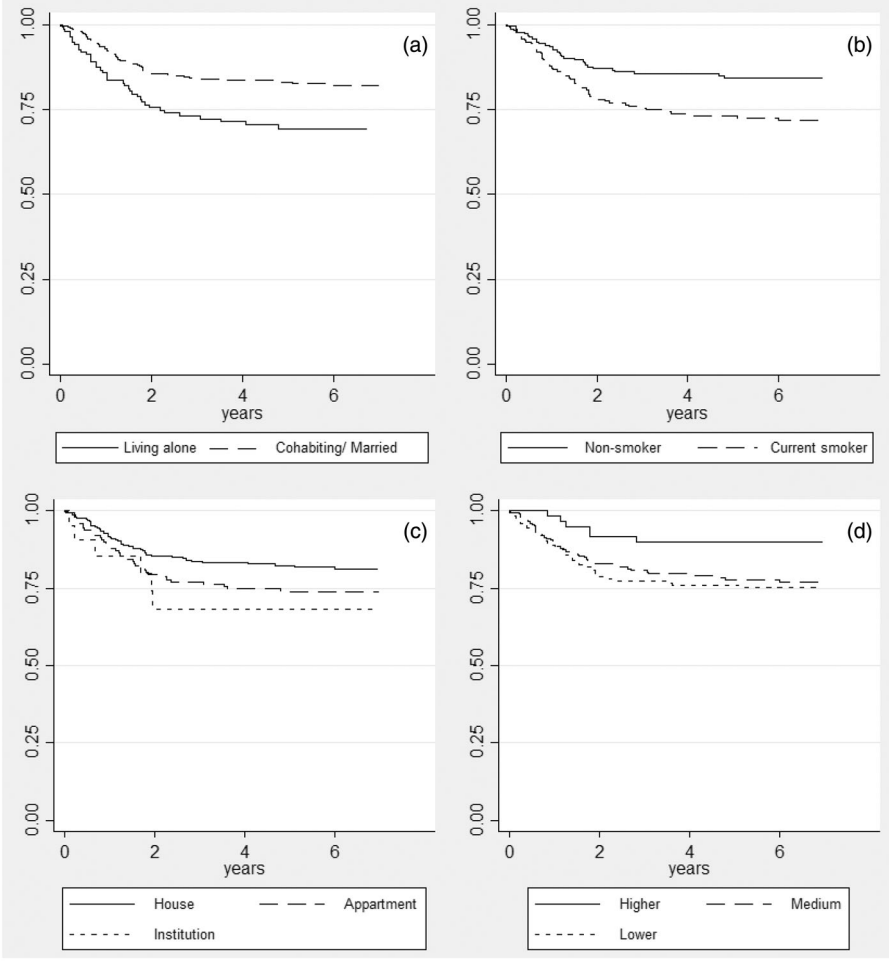

Figure 1. Penile cancer-specific Kaplan–Meier survival estimates for penile squamous cell carcinoma patients. (a) Cohabitation: dotted line, married or cohabiting patients; solid line, patients living alone. (b) Smoking status: dotted line, current smokers; solid line, non-smoking patients. (c) Living arrangements: solid line, living in a house; long dotted line, living in an apartment; short dotted line, living in institution. (d) Social groups: solid line, social groups 1–2; long dotted line, social groups 3–4; short dotted line, social groups 5–6.

significant association between cohabitation and socio-economic groups; pSCC patients who are cohabiting tend to be of higher socio-economic grouping. Socio-economic grouping had an independent prognostic value in higher and lower socio-economic groups even after adjusting for cohabiting status. At the current cohort size, we could not establish a significant association between living arrangements and cancer-specific survival.

Our finding of cohabiting as a predictor of survival in penile cancer is in line with previous studies on marital status [5–10] . These studies have examined cohabitation as a prognostic factor, Mao et al. had their cohabiting patients stratified even further into married, divorced, single and widowed and found the lowest cancer-specific survival (CSS) in the widowed patient group [15]. Another study by Thuret et al. has shown that unmarried present more often with worse stages of pSCC and cohabitation here had no effect on CSS [16]. In the current study, we found no significant difference in cohabitation status among different AJCC-stages. A previous Danish register study [17] by Ulff-Moller et al., which analyzed 1428 patients with invasive penile squamous cell carcinoma and cohabitation, found that divorced patients had poorer prognosis.

Cohabitation has demonstrated cancer-specific survival benefits in a large body of studies, while the underlying mechanism remains unknown [13]. Several studies have demonstrated that a strong social network such as ties to family, friends and spouses is associated with increased recovery rate and lower mortality [14–16].

Penile cancer is known to evade early detection. The delayed diagnosis may lead to a more advanced state at diagnosis and a worse prognosis. Living alone and lesser socio-economic conditions may lead to less hygienic conditions and worse self-care. While cohabitation and better socio-economic conditions have been hypothesized to lead to greater compliance with healthcare systems. In this study, there were no significant differences in clinical intervals between cohabiting patients and patients living alone. Social conditions such as living circumstances and socio-economic status have a general supportive effect on the individual [18,19]. These might be some of the underlying, mechanism tough more research is necessary.

It has been proposed that that cohabiting patients and patients in higher socio-economic groups have better access to healthcare and have a stronger financial situation [13]. Patients living alone also seem to experience more psychological stress and depression, which may have an effect on endocrine and immune responses thus leading to cancer progression [17,20].

Marriage and cohabitation functions as an important social support, which improves both compliance with health care systems and numerous physiological mechanisms with impact on health [18]. The spouse plays a critical role in health-specific behavior for the individual including monitoring, which may be related to early diagnosis [19]. It has indeed been demonstrated, that cohabiting patients are in better health than patients living alone [18].

The access to general healthcare is widely different throughout the world. A multicenter study from the USA by Attalla et al. found worse outcomes in both pathological staging and in CSS for patients with no healthcare insurance [21]. The Danish Health care system provides free general healthcare. Even so, our current study indicates that free access is insufficient to provide equal possibilities. We still find an association between social-economic groups and prognosis in penile carcinoma. Health inequality between different social groupings is still present in public systems providing free health-care.

Limitations and strengths

The main limitation of this study is the retrospective study design. However, our retrospective cohort represents a national dataset, which limits potential selection bias. Thorough and strict record-keeping tradition at all participating centres made the maintained data of great completeness and high quality. However, data on occupation was not consistently available, especially in retired patients.

Conclusion

Living alone and in poor socio-economic conditions predict poor prognosis in penile cancer in this national study. The trend of living arrangements to predict better outcomes for patients living in a house compared to patients living in apartments and institutions failed to reach statistical significance. We make the case for further research in efforts to minimize cancer inequality pSCC patients.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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