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Original Article

Non-surgical management vs active treatment in T1a renal cell carcinoma: a population-based study

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Objectives

To compare overall and cancer-specific survival for clinical (c)T1aN0M0 renal cell carcinoma (RCC) in patients treated with non-surgical management (NSM: surveillance and watchful waiting) or active treatment (surgery and ablative treatments).

Patients and methods

In this nationwide real-world population-based cohort study, data on clinical, demographic, and socioeconomic factors as well as tumour characteristics and cause of death were retrieved from the Renal Cell Carcinoma Database Sweden (RCCBaSe) for 3989 patients diagnosed with cT1aN0M0 RCC, 2011–2020 and treated with either NSM or active treatment. Differences in survival between NSM and active treated patients were analysed using standard and competing-risks Cox regression models.

Results

In total, 3727 (93.4%) patients underwent active treatments, while 262 patients (6.6%) were treated with NSM. Patients in the NSM group were significantly older and had a higher comorbidity burden. During a median follow-up time of 4.1 years, all-cause mortality was significantly higher among the NSM (38.9%) than the actively treated (10.9%) patients ($P < 0.001$), as was cancer-specific mortality (13.0% vs 3.4%, $P < 0.001$). Larger tumours, older age, male sex, increased comorbidity, being unmarried or widowed, having lower disposable income, and having clear cell or papillary RCC compared with chromophobe RCC were all independently associated with poorer overall and cancer-specific survival. One of the limitations is that treatment allocation was not randomised.

Conclusion

Non-surgical management of cT1aN0M0 RCC was associated with poorer survival compared with surgery/ablation and should be offered mainly for patients with limited life expectancy and indolent renal tumours.

Keywords

active surveillance, all-cause mortality, cancer-specific mortality, cohort study, kidney cancer, renal cell carcinoma, renal tumour biopsy, socioeconomic factors, surgery

Introduction

During the last few decades, the incidence of small renal masses (SRMs) has steadily increased, which is largely attributed to the ageing of the population and the widespread use of cross-sectional imaging [1–3]. While surgery remains the standard treatment for small RCCs, many exhibit indolent behaviour, making non-surgical management (NSM) such as surveillance and watchful waiting a suitable approach. The European Association of Urology (EAU) recommends NSM

for elderly and comorbid patients with RCC in cases in which the risks associated with surgery outweigh the benefits [4].

Despite these recommendations, the role of NSM of small RCCs remains a topic of debate. Some studies support the use of NSM in patients aged >70 years, emphasising that the competing risk of all-cause mortality (ACM) surpasses the risk of cancer-specific death [5,6]. A prospective study concluded that NSM offered non-inferior cancer-specific survival (CSS) compared with surgery and ablative treatments, among patients with SRMs [7]. Moreover, comorbidities and frailty have been linked to poorer perioperative and oncological outcomes, further strengthening the indication for NSM [8]. Conversely, conflicting evidence suggests that NSM undermines both overall survival (OS) and CSS among patients with RCC [9–12].

Although international guidelines encourage NSM for carefully selected patients, uncertainty remains regarding the long-term outcomes and patient selection. This underlines the need for further research to assess the oncological and survival outcomes of NSM compared with active treatments and identify predictive factors for cancer progression. Studies conducted using the Surveillance, Epidemiology, and End Results (SEER) database indicated that lower socioeconomic status entailed poorer survival in patients with RCC [13,14]. However, it remains unclear whether similar disparities exist within other health care systems.

Aim

To compare CSS and OS among patients with clinical (c) T1aN0M0 RCC treated with NSM (active surveillance and watchful waiting) and surgery or tumour ablation and identify factors predictive of mortality.

Patients and Methods

Design and Settings

This retrospective register-based cohort study was conducted using data from the Renal Cell Carcinoma Database Sweden (RCCBaSe), a comprehensive database containing demographic, socioeconomic and clinical data from multiple national Swedish registers on 17 107 patients (representing 17 628 tumours) diagnosed with RCC in Sweden and registered in the National Swedish Kidney Cancer Register (NSKCR) from its inception in 2004 to December 2020 [15]. We identified and included all patients diagnosed with cT1aN0M0 RCC during 2011–2020 and treated with NSM or active treatment. Patients with metastatic disease at diagnosis or missing data on key variables were excluded (Fig. 1), resulting in a total study population of 3989 unique individuals.

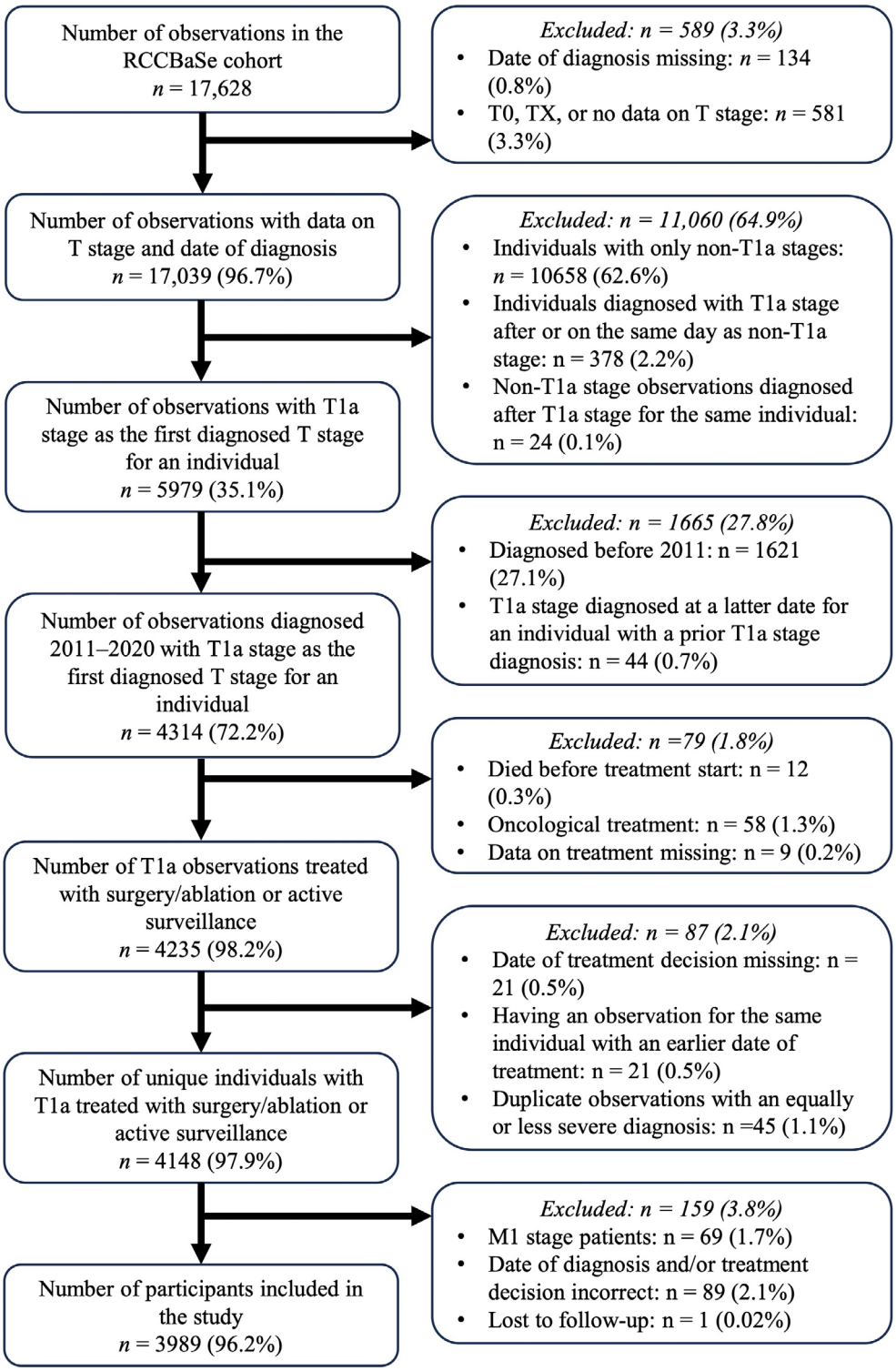
Study Variables

Demographic and clinical data collected from RCCBaSe included age at treatment decision, sex, education level, disposable income, marital and employment status, tumour size, tumour stage, histological subtype, treatment modality, comorbidities according to the Charlson Comorbidity Index (CCI), and cause of death. The CCI was calculated based on International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) codes registered during the 2 years before the date of treatment decision, with weights from Charlson et al. [16] (excluding ICD-10 code C64) and ICD-10 coding from Quan et al. [17].

Statistical Analyses

Categorical data are presented as frequencies and percentages, *n* (%), while discrete and continuous data are given as medians and interquartile ranges (IQRs), supplied with means (SDs). Tests of differences between the active treatment and NSM groups were performed using Pearson's chi-squared test for categorical data, the Mann–Whitney test for discrete data and Welch's *t*-test for continuous data. OS was illustrated with Kaplan–Meier plots, while tests of differences in OS between the active treatment and NSM groups were performed using log-rank tests. The association between treatment and time to death was estimated using adjusted and unadjusted Cox regression models for cancer-specific mortality (CSM) and ACM. Additionally, competing risks Cox regression models—both adjusted and unadjusted—were used to estimate the association between treatment and time to death for CSM, with the two possible outcomes being death from RCC and death from any other cause (non-RCC death). NSM was compared with active treatment (reference category), while age at time of treatment decision (years), male sex (yes/no), Swedish born (yes/no), college/university education (yes/no), disposable income (per €1000/year), marital status (married [reference category], unmarried, divorced, or widow/widower), Swedish cancer centre region (North, South, Southeast, Stockholm-Gotland [reference category], Uppsala-Örebro, or West), CCI excluding RCC (points), time from date of RCC diagnosis to date of treatment decision (years), right-sided RCC (yes/no), tumour size (mm), RCC type (chromophobe [reference category], clear cell, papillary, or other/unknown), and year of treatment decision were used as confounders. Regarding marital status, participants with a registered partnership were categorised as 'married', while participants with a dissolved registered partnership were categorised as 'divorced'. For yes/no dichotomous variables, 'no' was used as the reference category. Results from Cox regression analyses are

Fig. 1 Flow chart of the inclusion process for the 3989 patients with cT1aN0M0 RCC included in the present study.



presented as hazard ratios (HRs) with 95% CIs. All statistical analyses were performed using R 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria), with a two-sided $P < 0.05$ considered statistically significant.

Results

The demographic and clinical characteristics of the 3989 participants, of whom 3727 (93.4%) underwent active

treatment and 262 (6.6%) received NSM, are summarised in Table 1 [16,17]. Patients in the NSM group were significantly older, with a median (IQR) age of 74.4 (69.5–80.0) years compared with 66.6 (56.8–73.3) years ($P < 0.001$). Additionally, the NSM patients had a higher comorbidity burden, with a median (IQR) CCI of 2 (0–3) points compared with 0 (0–2) points in the active treatment group (P <0.001). Among the NSM patients, 102 (39%) were clinically diagnosed as RCC based on imaging and clinical examinations, without a morphological verification. In contrast, only four (0.1%) of the actively treated patients lacked histopathological verification. Further, median tumour size was significantly smaller in the NSM patients.

Table 1 Characteristics of the 3989 patients with cT1aN0M0 RCC included in the present study.

Variable	Total	Treatment		*P*
	***N* = 3989**	**Active treatment *n* = 3727 (93.4%)**	**NSM *n* = 262 (6.6%)**	
Time to follow-up, years				
Mean (SD)	4.4 (2.5)	4.5 (2.5)	3.1 (2.2)	N/A
Median (IQR)	4.1 (2.2–6.3)	4.2 (2.3–6.3)	2.5 (1.2–4.4)	
Status at follow-up, *n* (%)				
Censored	3482 (87.3)	3322 (89.1)	160 (61.1)	**<0.001**§
Deceased	507 (12.7)	405 (10.9)	102 (38.9)	
RCC death	160 (4.0)	126 (3.4)	34 (13.0)	
Non-RCC death	347 (8.7)	279 (7.5)	68 (26.0)	
Age at date of treatment decision, years				
Mean (SD)	65.1 (11.9)	64.4 (11.8)	73.8 (9.9)	**<0.001**¶
Median (IQR)	67.3 (57.5–73.8)	66.6 (56.8–73.3)	74.4 (69.5–80.0)	
Male sex, *n* (%)	2528 (63.4)	2368 (63.5)	160 (61.1)	0.462‖
Swedish-born, *n* (%)	3223 (80.8)	3011 (80.8)	212 (80.9)	1.000‖
College/university education, *n* (%)	1002 (25.1)	943 (25.3)	59 (22.5)	0.352‖
Disposable income, €1000/year*				
Mean (SD)	25.7 (31.6)	26.1 (32.4)	20.2 (14.5)	**<0.001**¶
Median (IQR)	19.5 (14.3–29.2)	20.0 (14.4–29.6)	16.8 (13.5–20.9)	
Marital status, *n* (%)†				
Married	2245 (56.3)	2103 (56.4)	142 (54.2)	**<0.001**‖
Unmarried	698 (17.5)	662 (17.8)	36 (13.7)	
Divorced	727 (18.2)	686 (18.4)	41 (15.6)	
Widow/widower	319 (8.0)	276 (7.4)	43 (16.4)	
Cancer centre region, *n* (%)				
North	335 (8.4)	321 (8.6)	14 (5.3)	**<0.001**‖
South	720 (18.0)	667 (17.9)	53 (20.2)	
Southeast	483 (12.1)	462 (12.4)	21 (8.0)	
Stockholm-Gotland	904 (22.7)	858 (23.0)	46 (17.6)	
Uppsala-Örebro	901 (22.6)	809 (21.7)	92 (35.1)	
West	646 (16.2)	610 (16.4)	36 (13.7)	
CCI excluding RCC, points‡				
Mean (SD)	1.04 (1.72)	0.94 (1.60)	2.35 (2.60)	**<0.001****
Median (IQR)	0 (0–2)	0 (0–2)	2 (0–3)	
0 points, *n* (%)	2297 (57.6)	2219 (59.5)	78 (29.8)	
1 point, *n* (%)	558 (14.0)	521 (14.0)	37 (14.1)	
2 points, *n* (%)	638 (16.0)	576 (15.5)	62 (23.7)	
≥3 points, *n* (%)	496 (12.4)	411 (11.0)	85 (32.4)	
Time from date of RCC diagnosis to date of treatment decision, days				
Mean (SD)	80 (131)	75 (124)	138 (203)	**<0.001**¶
Median (IQR)	43 (22–85)	42 (22–82)	78 (36–137)	
Right-sided RCC, *n* (%)	2028 (50.8)	1902 (51.0)	126 (48.1)	0.373‖
Tumour size, mm				
Mean (SD)	27.3 (9.8)	27.5 (9.9)	24.7 (9.0)	**<0.001**¶
Median (IQR)	27 (20–35)	28 (20–35)	24 (18–30)	
RCC type, *n* (%)				
Chromophobe	329 (8.2)	320 (8.6)	9 (3.4)	**<0.001**‖
Clear cell	2661 (66.7)	2559 (68.7)	102 (38.9)	
Papillary	732 (18.4)	695 (18.6)	37 (14.1)	
Other/unknown	267 (6.7)	153 (4.1)	114 (43.5)	

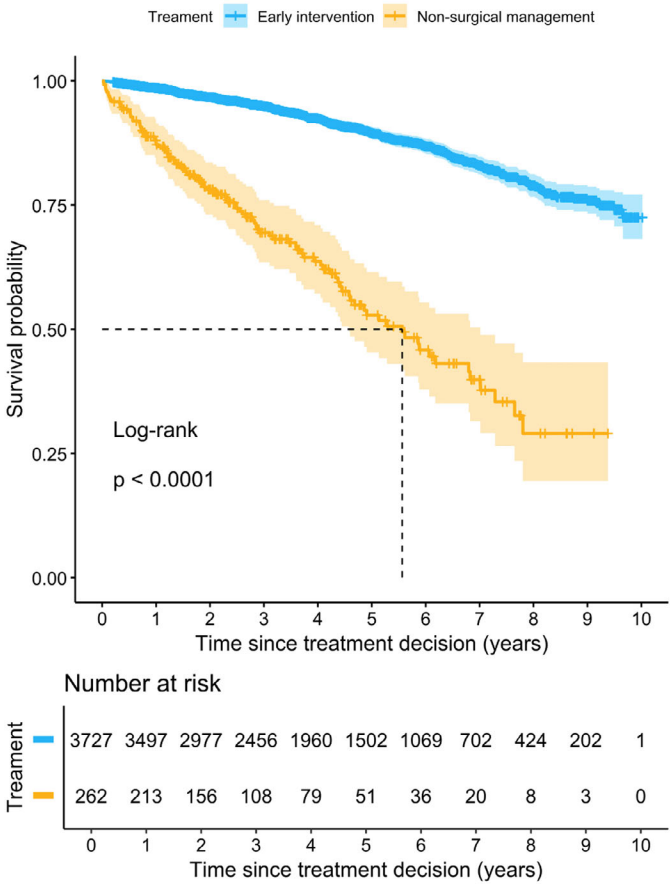
*Significant P values are given in bold. N/A, not applicable. *Missing values for disposable income: one (0.03%); right-sided RCC: eight (0.2%) participants. †Participants with a registered partnership (three [0.08%]) were categorised as 'married', while participants with a dissolved registered partnership (one [0.03%]) were categorised as 'divorced'. ‡Calculated based on ICD-10 codes registered during the 2 years before the date of treatment decision, with ICD-10 coding according to Quan et al. [17] and weights from Charlson et al. [16], excluding ICD-10 code C64. §P values from log-rank test. ¶P values from Welch's t-test. ‖P values from Pearson's chi-squared test. **P values from the Mann–Whitney test.*

In total, 507 (12.7%) deaths occurred during a median (IQR) of 4.1 (2.2–6.3) years of follow-up, 102 (38.9%) of the NSM patients and 405 (10.9%) of the actively treated patients. Univariate analyses showed a significant difference in ACM between the NSM and active treatment patients (log-rank test $P < 0.001$), with considerably higher ACM in the NSM patients during the follow-up period (Fig. 2). RCC-specific mortality accounted for 160 (4.0%) deaths, 34 (13.0%) of the NSM patients and 126 (3.4%) of the actively treated patients.

Cancer-Specific Survival

Results from competing risks Cox regression models for time to death from RCC or any other cause (non-RCC) are given in Table 2 [16,17] and Fig. 3. NSM patients had a 5.85 times higher unadjusted risk of RCC-specific death compared with the actively treated patients, with an adjusted HR of 3.32 (95% CI 2.03–5.44, $P < 0.001$). Several other factors were also independently associated with CSS in the adjusted analyses, with each additional year of age implying a 5% increase in CSM ($P < 0.001$), male sex entailing a 70% higher risk of CSM ($P = 0.006$), and each additional CCI point resulting in a 20% increase in CSM ($P < 0.001$). Moreover, each additional millimetre in tumour diameter corresponded to a 1% increase in the risk of RCC-specific death ($P < 0.001$). At the same time, patients with clear cell and papillary RCC had 11.9-fold ($P = 0.013$) and 9.9-fold ($P = 0.023$) increased risks of RCC-specific death, respectively, compared with patients with chromophobe RCC.

Fig. 2 Kaplan–Meier plot with 95% CIs for the outcome ACM during the 10 years after treatment decision for participants undergoing active treatment or NSM.



Overall Survival

Results from Cox regression models for time to death from any cause (ACM) are given in Table 3 [16,17]. Compared with the active treatment group, the NSM group had a 5.7 times higher unadjusted risk of death from any cause ($P < 0.001$), while the adjusted risk was 2.3 times higher ($P < 0.001$). Moreover, in the adjusted analyses, each additional year of age increased the risk of death from any cause by 6% ($P < 0.001$), and male sex increased the risk by 24% ($P = 0.031$). In comparison, each 1-point increase in CCI was associated with a 25% higher risk of death from any cause ($P < 0.001$). Additionally, each millimetre increase in tumour diameter resulted in a 1% higher ACM ($P < 0.001$).

Socioeconomic and Geographic Factors

While patients with a college degree had a significantly lower ACM during follow-up, HR 0.76 ($P = 0.028$) in the adjusted analyses, unmarried and widowed individuals had a significantly higher ACM, HR 1.39 ($P = 0.018$) and 1.46 ($P = 0.006$), respectively, compared with married patients. However, no significant associations with CSS were observed for education level or marital status.

In the adjusted analyses, each €1000/year increase in disposable income implied a 3% reduction in the risk of RCC-specific death ($P < 0.001$), although no significant association with OS was observed. However, country of birth did not significantly influence either CSS or OS in the adjusted analyses.

Compared with the reference region of Stockholm-Gotland, patients treated in the South region of Sweden had significantly lower ACM in the adjusted analyses, HR 0.73 ($P = 0.036$). No significant differences between geographic regions were observed for CSS.

Discussion

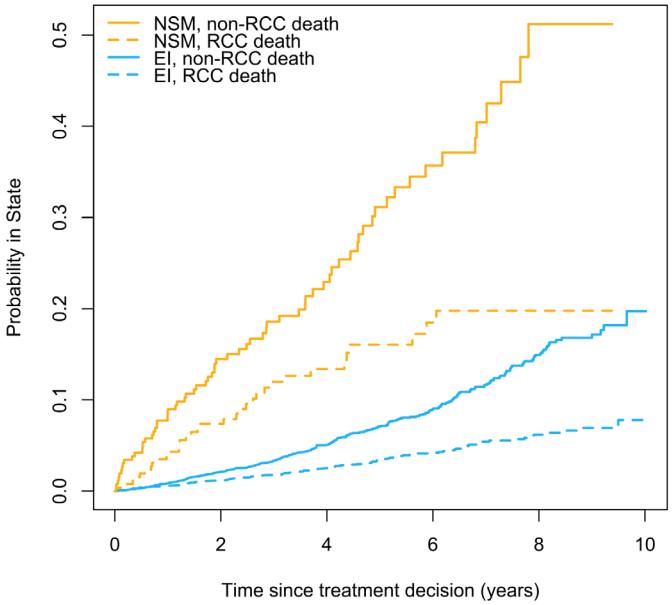
This study indicated that NSM of cT1aN0M0 RCC was associated with poorer survival outcomes than was surgery or ablation. Furthermore, age, sex, comorbidity, tumour characteristics, and socioeconomic factors predicted survival.

Table 2 Results from adjusted and unadjusted competing risks Cox regression models for time to death from RCC (CSM) for the 3989 patients with cT1aN0M0 RCC included in the present study.

Event	Variable	Unadjusted		Adjusted*	
		HR (95% CI)	*P*	HR (95% CI)	*P*
Death from RCC	NSM	5.85 (3.98–8.59)	<**0.001**	3.32 (2.03–5.44)	<**0.001**
	Age at time of treatment decision (years)	1.08 (1.05–1.10)	<**0.001**	1.05 (1.03–1.08)	<**0.001**
	Male sex	1.19 (0.85–1.66)	0.299	1.70 (1.16–2.48)	**0.006**
	Swedish-born	1.78 (1.09–2.91)	**0.021**	1.57 (0.91–2.71)	0.105
	College/university education	0.82 (0.55–1.20)	0.298	1.25 (0.83–1.88)	0.272
	Disposable income (€1000/year)	0.96 (0.95–0.98)	<**0.001**	0.97 (0.95–0.99)	<**0.001**
	Marital status†				
	Married	Ref.		Ref.	
	Unmarried	0.60 (0.35–1.03)	0.061	0.83 (0.47–1.45)	0.516
	Divorced	1.15 (0.76–1.72)	0.509	1.27 (0.82–1.96)	0.287
	Widow/widower	1.62 (0.99–2.63)	0.051	1.09 (0.64–1.82)	0.753
	Cancer centre region				
	North	1.23 (0.65–2.32)	0.526	0.90 (0.46–1.74)	0.751
	South	1.28 (0.77–2.09)	0.334	0.94 (0.54–1.60)	0.806
	Southeast	1.03 (0.57–1.85)	0.911	0.83 (0.44–1.55)	0.563
	Stockholm-Gotland	Ref.		Ref.	
	Uppsala-Örebro	1.19 (0.73–1.92)	0.479	0.92 (0.53–1.58)	0.764
	West	1.16 (0.69–1.96)	0.572	0.99 (0.57–1.73)	0.983
	CCI excluding RCC (points)‡	1.29 (1.23–1.37)	<**0.001**	1.20 (1.12–1.28)	<**0.001**
	Time from date of RCC diagnosis to date of treatment decision (days)	1.47 (1.09–1.97)	**0.009**	0.98 (0.64–1.49)	0.931
	Right-sided RCC	1.25 (0.91–1.71)	0.167	1.29 (0.93–1.77)	0.116
	Tumour size (mm)	1.01 (1.00–1.02)	<**0.001**	1.01 (1.00–1.03)	<**0.001**
	RCC type				
	Chromophobe	Ref.		Ref.	
	Clear cell	13.91 (1.94–99.50)	**0.009**	11.86 (1.67–83.71)	**0.013**
	Papillary	12.25 (1.66–89.96)	**0.014**	9.93 (1.36–72.34)	**0.023**
	Other/unknown	21.94 (2.88–166.97)	**0.003**	7.06 (0.92–54.20)	0.060
	Year of treatment decision	1.03 (0.95–1.12)	0.471	1.04 (0.95–1.13)	0.364
Death from non-RCC	NSM	5.64 (4.29–7.41)	<**0.001**	2.03 (1.41–2.91)	<**0.001**
	Age at time of treatment decision (years)	1.08 (1.06–1.10)	<**0.001**	1.06 (1.04–1.08)	<**0.001**
	Male sex	0.85 (0.68–1.06)	0.140	1.10 (0.86–1.41)	0.447
	Swedish-born	1.24 (0.92–1.67)	0.146	0.91 (0.66–1.25)	0.549
	College/university education	0.46 (0.33–0.64)	<**0.001**	0.59 (0.43–0.81)	<**0.001**
	Disposable income (€1000/year)	0.98 (0.96–1.00)	**0.031**	1.00 (0.98–1.01)	0.340
	Marital status†				
	Married	Ref.		Ref.	
	Unmarried	1.15 (0.84–1.56)	0.383	1.71 (1.23–2.36)	**0.001**
	Divorced	1.13 (0.83–1.53)	0.430	1.12 (0.81–1.56)	0.489
	Widow/widower	2.92 (2.21–3.86)	<**0.001**	1.66 (1.18–2.34)	**0.003**
	Cancer centre region				
	North	1.03 (0.68–1.55)	0.900	0.82 (0.52–1.27)	0.363
	South	0.80 (0.56–1.13)	0.204	0.64 (0.44–0.93)	**0.017**
	Southeast	0.80 (0.54–1.19)	0.264	0.66 (0.44–0.99)	**0.043**
	Stockholm-Gotland	Ref.		Ref.	
	Uppsala-Örebro	1.05 (0.77–1.43)	0.750	0.80 (0.58–1.12)	0.189
	West	0.85 (0.59–1.21)	0.357	0.73 (0.50–1.07)	0.099
	CCI excluding RCC (points)‡	1.33 (1.28–1.39)	<**0.001**	1.28 (1.22–1.34)	<**0.001**
	Time from date of RCC diagnosis to date of treatment decision (days)	1.61 (1.35–1.91)	<**0.001**	1.27 (1.01–1.61)	**0.040**
	Right-sided RCC	1.17 (0.94–1.45)	0.156	1.14 (0.91–1.43)	0.230
	Tumour size (mm)	1.01 (1.00–1.02)	<**0.001**	1.01 (1.01–1.02)	<**0.001**
	RCC type				
	Chromophobe	Ref.		Ref.	
	Clear cell	1.30 (0.81–2.09)	0.269	1.11 (0.69–1.78)	0.665
	Papillary	1.59 (0.95–2.65)	0.073	1.43 (0.85–2.38)	0.169
	Other/unknown	4.32 (2.52–7.40)	<**0.001**	1.89 (1.04–3.45)	**0.037**
	Year of treatment decision	1.03 (0.97–1.10)	0.272	1.02 (0.96–1.09)	0.464

*Significant P values are given in bold. Ref., reference category. *Results based on n = 3980 (99.8%) participants with n = 506 (12.7%) events and concordance (standard error) 0.792 (0.011). †Participants with a registered partnership were categorised as 'married', while participants with a dissolved registered partnership were categorised as 'divorced'. ‡Calculated based on ICD-10 codes registered during the 2 years before the date of treatment decision, with ICD-10 coding according to Quan et al. [17] and weights from Charlson et al. [16], excluding ICD-10 code C64.*

Fig. 3 Probability of being in any of the two possible states, death from RCC or death from any other cause (non-RCC), during the 10 years after treatment decision for participants undergoing active treatment or NSM.



Our findings are consistent with those reported by Zini et al. [9] from the largest population-based study comparing NSM and nephrectomy for SRMs. In their cohort of 10 291 patients, NSM was associated with significantly worse CSS and OS, with a 9.4% decrease in 5-year survival among NSM patients. As was observed in our study, age and tumour size were significant independent predictors of CSS.

The negative impact of NSM on survival identified in the present study was also reported in the population-based study by Xing et al. [10]. While surgery and thermal ablation were associated with an increased risk of adverse events, including secondary malignancies and renal, cardiovascular, thromboembolic, and infectious complications, they were nonetheless linked to better OS and CSS compared with a non-surgical approach. Similarly, two systematic reviews and meta-analyses indicated that partial nephrectomy and thermal ablation were associated with significantly better OS and CSS when compared with active surveillance for patients with SRMs [11,12]. In a recent systemic review, Tsuboi et al. [18] observed this survival difference comparing active surveillance with surgery and ablation for SRMs. However, the difference in survival disappeared when the included SEER data were

Table 3 Results from adjusted and unadjusted Cox regression models for time to death from any cause (ACM) for the 3989 patients with cT1aN0M0 RCC included in the present study.

Variable	Unadjusted		Adjusted*	
	HR (95% CI)	*P*	HR (95% CI)	*P*
NSM	5.71 (4.58–7.11)	**<0.001**	2.39 (1.81–3.15)	**<0.001**
Age at time of treatment decision (years)	1.08 (1.06–1.09)	**<0.001**	1.06 (1.04–1.07)	**<0.001**
Male sex	0.94 (0.78–1.13)	0.526	1.24 (1.02–1.51)	**0.031**
Swedish-born	1.38 (1.07–1.78)	**0.012**	1.06 (0.81–1.38)	0.672
College/university education	0.57 (0.44–0.73)	**<0.001**	0.76 (0.59–0.98)	**0.028**
Disposable income (€1000/year)	0.98 (0.96–0.99)	**<0.001**	0.99 (0.98–1.00)	**0.017**
Marital status†				
Married	Ref.		Ref.	
Unmarried	0.95 (0.73–1.24)	0.718	1.39 (1.05–1.83)	**0.018**
Divorced	1.14 (0.89–1.45)	0.301	1.16 (0.90–1.49)	0.233
Widow/widower	2.46 (1.92–3.15)	**<0.001**	1.46 (1.11–1.92)	**0.006**
Cancer centre region				
North	1.08 (0.76–1.53)	0.658	0.84 (0.58–1.21)	0.341
South	0.93 (0.70–1.24)	0.611	0.73 (0.54–0.99)	**0.036**
Southeast	0.87 (0.62–1.20)	0.381	0.72 (0.51–1.01)	0.051
Stockholm-Gotland	Ref.		Ref.	
Uppsala-Örebro	1.09 (0.84–1.41)	0.516	0.84 (0.64–1.11)	0.212
West	0.93 (0.70–1.25)	0.643	0.81 (0.60–1.10)	0.170
CCI excluding RCC (points)‡	1.32 (1.27–1.36)	**<0.001**	1.25 (1.21–1.30)	**<0.001**
Time from date of RCC diagnosis to date of treatment decision (days)	1.57 (1.31–1.87)	**<0.001**	1.18 (0.95–1.47)	0.130
Right-sided RCC	1.19 (0.99–1.42)	0.051	1.18 (0.99–1.41)	0.064
Tumour size (mm)	1.01 (1.00–1.02)	**<0.001**	1.01 (1.00–1.02)	**<0.001**
RCC type				
Chromophobe	Ref.		Ref.	
Clear cell	1.93 (1.23–3.04)	**0.004**	1.65 (1.04–2.61)	**0.030**
Papillary	2.13 (1.31–3.45)	**0.002**	1.84 (1.13–3.00)	**0.014**
Other/unknown	5.17 (3.11–8.60)	**< 0.001**	2.03 (1.17–3.51)	**0.011**
Year of treatment decision	1.03 (0.98–1.08)	0.195	1.03 (0.98–1.08)	0.250

*Significant P values are given in bold. Ref., reference category. *Results based on n = 3980 (99.8%) participants with n = 506 (12.7%) events and concordance (standard error) 0.784 (0.011). †Participants with a registered partnership were categorised as 'married', while participants with a dissolved registered partnership were categorised as 'divorced'. ‡Calculated based on ICD-10 codes registered during the 2 years before the date of treatment decision, with ICD-10 coding according to Quan et al. [17] and weights from Charlson et al. [16], excluding ICD-10 code C64.*

eliminated, illustrating the heterogeneity between population-based and institutional studies, possibly reflecting selection biases. Our population-based results align with the SEER-based findings in that study, showing the value of analysing large population-based real-world data. Ablative therapy has been shown to carry a higher risk of local and distant recurrence compared with surgery [19].

These consistent findings across multiple studies suggest that active treatment, whether ablation or surgery, offers survival benefits compared with NSM. In contrast, several studies suggest that surgical treatment of localised RCC has no survival benefits for older patients. Lane et al. [5], in a retrospective single-centre study including 537 patients with T1 renal tumours who underwent radical nephrectomy, partial nephrectomy or surveillance, reported that interventions were not significantly associated with improvements in OS among patients aged >75 years. However, increasing age and comorbidity were significantly associated with ACM, with the most common cause of death being cardiovascular disease, as in the general elderly population. Nephrectomy accelerated renal dysfunction, which in turn was associated with cardiovascular mortality. Similarly, Hollingsworth et al. [6] reported that despite surgical treatment, the estimated 5-year competing-risk mortality in patients aged >70 years was 28.2%. These findings support the consideration of NSM as a therapeutic approach for selected elderly patients with limited life expectancy, significant comorbidities, or indolent RCC types. Tumour histology might preferably be considered before NSM, as chromophobe RCC generally has a more favourable course compared with clear cell and papillary RCC.

In our study, 39% of the NSM patients lacked morphological verification of their diagnosis. The absence of morphology brings a risk for misclassification, as a proportion of these SRMs may have been benign. Previous studies have estimated that up to one-third of SRMs are benign [1,20]. This suggests that the survival disadvantage of NSM may be even greater than observed, owing to the possible admixture of benign tumours in the NSM group, mitigating the survival disadvantage of NSM treatment. This underlines the importance of renal tumour biopsy (RTB) before treatment decisions concerning SRMs [21,22]. RTB is a safe and accurate diagnostic tool that enables histopathological characterisation of SRMs, reduces the risk of overtreatment, and facilitates a more individualised management approach [1,23]. RTB is cost-effective in handling SRMs, avoiding unnecessary treatment and follow-up [24].

The present study is a population-based study exploring the impact of socioeconomic factors on survival for patients with RCC. We observed that male sex, unmarried status, lower education, and lower income were all significantly associated with poorer survival rates. These findings are consistent with studies based on the SEER database, which have similarly reported that male sex, lower income, and being unmarried are linked to reduced survival in patients with RCC [13,14]. Also a comparable Danish study by Eriksen et al. [25], including 2941 patients with RCC, demonstrated similar results, with lower disposable income, lower educational level, and weaker labour market affiliation associated with poorer survival rates. Married men and cohabiting/married women enjoyed higher survival rates than other groups, as was observed in our study. Notably, in the Danish study, male immigrants and their descendants had better survival rates than men of Danish origin. This finding was not confirmed for the Swedish population in the present study.

The observed disparities in survival by socioeconomic factors highlight the need to address underlying inequalities in access to health care and health literacy. These disparities also warrant increased support, patient education, and guidance for socioeconomically vulnerable groups.

We identified some significant regional variations in OS among patients with cT1aN0M0 RCC. However, there were no significant differences in CSS, suggesting that these disparities may be related to other health care system factors, variation in access to health care or differences in the general population's health. Further investigations are needed to understand the underlying causes of these geographic differences.

The role of NSM has been widely debated, and the lack of prospective randomised controlled trials limits the strength of available evidence. Given this shortcoming, clinical decision-making must continue to rely on observational real-world studies such as ours. Our findings suggest that NSM of RCC undermines survival and should be offered selectively, mainly for patients with limited life expectancy and RTB should be considered before management of SRMs [1,23,24]. Treatment decisions should also consider clinical, demographic, and socioeconomic prognostic factors.

This study has several limitations inherent to its register-based design. Treatment allocation was not randomised, raising the risk of selection bias, with patients managed by NSM being older and more comorbid. The relatively short median follow-up of 4.1 years in patients with cT1a RCC might be a limitation as these tumours often have an indolent behaviour. Any overestimation of CSM might have contributed to an increased CSM in our study. However, data on cause of death was for all patients retrieved from the Swedish Cause of Death Register and should thus be reliable.

Despite adjustments for demographic, clinical and socioeconomic factors, residual confounding from unmeasured variables such as performance status and smoking history cannot be excluded. Survival was measured from the date of treatment decision rather than the date of diagnosis. The longer period between diagnosis and treatment

decision in the NSM group may have led to an underestimation of survival in this group. Furthermore, while the results are based on a large national cohort, they may not be generalisable to settings with different health care systems, resources, or demographics.

In conclusion, NSM of cT1aN0M0 RCC was associated with poorer survival outcomes compared with surgery or ablation. Also, age, sex, comorbidity, tumour characteristics, and socioeconomic factors predicted survival outcomes. NSM is primarily appropriate for patients with limited life expectancy and indolent renal tumours.

Disclosure of Interests

All authors declare no competing interests.

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Abbreviations: ACM, all-cause mortality; CCI, Charlson Comorbidity Index; CSM, cancer-specific mortality; CSS, cancer-specific survival; cT, clinical T stage; HR, hazard ratio; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision; IQR, interquartile range; NSM, non-surgical management; OS, overall survival; RCCBaSe, Renal Cell Carcinoma Database Sweden; RTB, renal tumour biopsy; SEER, Surveillance, Epidemiology, and End Results; SRM, small renal mass.

