Medical and non-medical determinants of prostate cancer management: a population-based study

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Abstract

Non-medical factors influencing treatment choices in prostate cancer are not well understood. We carried out a population-based study to obtain information on the management of prostate cancer patients. Our study population consisted of 1000 men diagnosed during 1995 from five French cancer registries. We looked at the main treatments performed in the year following diagnosis. Multivariate analysis was used to describe the determinants of the various treatment choices, simultaneously taking into account medical and non-medical factors. The probability of treatment by radical prostatectomy (RP) was 3 times higher in the Tarn area, whereas in the Calvados area the probability of treatment by radiotherapy was almost 6 times higher. The private sector favoured radical prostatectomy and hormonal therapy. In France, as in other developed countries, the initial treatment of prostate cancer varies greatly according to non-medical factors. This type of investigation, if carried out regularly, would make it possible to evaluate changes in practice patterns.
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1. Introduction

Prostate cancer is the most frequently diagnosed cancer among men in developed countries. In most European countries, the incidence of prostate cancer has risen more than that of any other cancer over the past two decades, mainly due to the increasing use of prostate-specific antigen (PSA) testing and ultrasonography. In France, crude incidence was estimated at 93.7 per 100 000 person-years in 1995 [1] (age-standardised rate using the world population as a standard: 54.4/100 000). Although prostate cancer can be screened for by PSA testing, the optimal management of the disease is still controversial [2].

Strategies for treatment of prostate carcinoma show variation not only between different countries, but also from one region to another within a given country [3,4]. Treatment efficacy can only be assessed through randomised clinical trials using large series. Such studies are underway, but their results will not be available for several years [5]. In the interim, we have to rely on observational or registry studies to evaluate the results of prostate carcinoma care.

In the French population, non-medical determinants of the variation of treatment choices in prostate cancer are not very well understood. We carried out a population-based study to obtain information on practice patterns in prostate cancer management during 1995 in five French cancer registries. We also aimed to reveal any variations between the regions and sectors by the unbiased evaluation of treatment practices in France.

2. Patients and methods

2.1. Population

Our study population consisted of 1000 men with a prostate neoplasm diagnosed during 1995 in five of the eight French cancer registries covering the following

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administrative areas: Bas-Rhin, Calvados, Haut-Rhin, Isère and Tarn. A sample of 200 randomly selected cases from the database of each registry was considered to be representative of the number of prostate cancers diagnosed annually in these regions. Definitive analysis concerned only 991 patients as nine cases were excluded because the prostate neoplasm was a fortuitous discovery after radical cystoprostatectomy for bladder neoplasm. These five areas, chosen because of their wide geographical distribution around the country, differed in their urbanisation and healthcare distribution. In 1995, they represented 3.7 million inhabitants (approximately 7% of the French population).

2.2. Data

In 1998, the social and demographic characteristics of the patient, diagnostic circumstances, histological and clinical characteristics of the tumour, treatment procedures and laboratory test results were collected retrospectively from the medical records by investigators from each registry. The clinical stage of the tumour was coded after a centralised review of all the questionnaires, based on the Tumour-Node-Metastasis classification in use at the time (TNM, 1992). Main therapies performed in the year following diagnosis were: radical prostatectomy whatever the associated treatment, radiotherapy with curative intent with or without hormonal therapy, hormonal therapy only, or watchful waiting including transurethral resection.

2.3. Statistical analysis

To identify the factors determining the initiation of each principal treatment modality, we used a bivariate analysis (Chi-square tests) in order to study the frequency of these treatments according to medical and non-medical determinants. Multivariate analysis by logistic regression was used to describe the determinants of the various treatment choices, simultaneously taking into account non-medical determinants (area of residence and physician's sector of activity) adjusted for

Table 1
Variations in medical determinants and sector of activity according to patients' area of residence

	Bas-Rhin	Calvados	Isère	Haut-Rhin	Tarn	Five areas	P value[a]
Incidence rate[b]	58.7	56.6	55.5	54.2	55.3	–	
Mortality rate[b]	16.8	19.2	14.3	16.5	12.3	–	
Sector of activity (%)							0.001
Public	44	22	23	66	18	35	
Private	56	78	77	34	82	65	
Age in years (%)							0.240
<60	9	9	6	6	6	7	
60–69	35	38	32	32	37	35	
70–79	35	39	36	42	38	38	
≥80	21	14	26	20	19	20	
PSA level in ng/ml (%)							0.004
<4	5	7	7	1	8	6	
4–9	21	13	11	14	22	16	
10–19	19	23	22	22	23	22	
≥20	40	46	43	47	38	43	
Unknown	15	11	17	16	9	13	
Gleason score (%)							0.001
2–6	67	56	52	73	48	59	
7	13	21	24	11	35	21	
8–10	15	20	21	13	14	17	
Unknown	5	3	3	3	3	3	
Clinical stage at diagnosis (%)							0.001
T1	27	29	23	11	26	23	
T2	36	30	35	39	36	35	
T3-4; N+	16	16	17	23	18	18	
M+	17	16	13	26	15	17	
Unknown	4	9	12	1	5	7	
Total cases	205	199	196	194	197	991	

N+, node-positive; M+, metastases; PSA, prostate-specific antigen.
[a] P value from Ch square test.
[b] Age-standardised rate/100 000 over the period 1993–1997, using the world population as a standard (French Network registry data, in press in 'Progrès en Urologie').

medical factors (age, PSA levels, clinical staging and Gleason score). In this model, the results were expressed as an adjusted odds ratio (aOR) which reflected the probability of receiving the treatment studied for a given category of patients compared with another group of patients who were considered as the reference category. For non-medical determinants, the Bas-Rhin area and the public sector were chosen as the reference categories. For medical determinants, the reference categories were age less than 60 years, PSA level below 4 ng/dl, Gleason score 2–6 and clinical stage T1N0M0. The analysis was performed using Stata software [6].

3. Results

In Table 1, areas of residence are compared according to medical and non-medical criteria. Incidence changed very little from one area to another, whereas the standardised mortality rate (using the world population as a standard) varied from 12.3 to 19.2/100 000 inhabitants per year. Age at diagnosis did not differ between the various administrative areas, although variations existed in the PSA level, Gleason score and clinical stage at diagnosis (the Haut-Rhin area had a higher incidence of metastatic patients).

208 patients (21%) received radical prostatectomy (Table 2), alone (15%) or associated with another treatment (6%). For 18% of patients, the initial treatment chosen was radiotherapy with curative intent, while only 5% were treated with combined radiotherapy and hormonal therapy. Hormonal therapy alone was administered to 37% of patients and almost 23% received no specific therapy. In 1% of patients, we had no information about the treatment given.

The medical factors determining the initial treatment received by our cohort were generally as expected (Tables 3–6). Initial treatment by radical prostatectomy was performed in young patients with localised, clinically

Table 2
Main treatments during the first year after diagnosis

Main treatment	Details of treatment	Population (%)
Radical prostatectomy (RP)		
	RP	153 (15.4)
	RP + Rx	26 (2.6)
	RP + H	25 (2.5)
	RP + Rx + H	4 (0.4)
	Total RP	208 (21.0)
Local radiotherapy (Rx)		
	Rx	99 (10.0)
	Rx + H	35 (3.5)
	Rx + TUR	33 (3.3)
	Rx + H + TUR	13 (1.3)
	Total Rx	180 (18.2)
Hormonal therapy (H)		
	H	244 (24.6)
	H + TUR	123 (12.4)
	Total H	367 (37.0)
Watchful waiting (WW) or transurethral resection (TUR)		
	WW	87 (8.8)
	TUR	140 (14.1)
	No specific therapy	227 (22.9)
Treatment unknown		9 (0.9)
Total		991 (100)

Table 3
Variations in choice of radical prostatectomy (RP) according to medical and non-medical determinants

	Univariate analysis		Multivariate analysis	
	% of RP	OR	aOR	95% CI
Area				
Bas-Rhin[ref]	16.1	1.0	1.0	–
Calvados	19.1	1.2	0.9	0.5–1.8
Isère	16.3	1.0	0.9	0.4–1.7
Haut-Rhin	17.0	1.1	1.7	0.8–3.4
Tarn	36.6	3.0	3.0	1.6–5.6
P value	0.001[a]			0.0001[b]
Sector				
Public[ref]	12.9	1.0	1.0	–
Private	25.3	2.3	2.6	1.5–4.2
P value	0.001[a]			0.0002[b]
Age				
<60[ref]	50.0	1.0	1.0	–
60–69	34.9	0.5	0.3	0.1–0.6
70–79	13.4	0.2	0.1	0.0–0.1
⩾80	0.5	0.0	0.0	0.0–0.0
P value	0.001[a]			0.0001[b]
PSA level				
<4[ref]	17.9	1.0	1.0	–
4–9	38.0	2.8	2.9	1.2–7.0
10–19	36.9	2.7	3.6	1.5–8.9
⩾20	10.6	0.6	1.5	0.6–3.6
Unknown	9.0	0.5	1.9	0.6–5.8
P value	0.001[a]			0.002[b]
Gleason score				
2–6[ref]	21.3	1.0	1.0	–
7	31.2	1.7	3.0	1.8–5.0
8–10	11.6	0.5	1.0	0.5–2.1
Unknown	0.0	0.0	0.0	0.0–0.0
P value	0.001[a]			0.0001[b]
Clinical stage				
T1[ref]	17.9	1.0	1.0	–
T2	40.8	3.2	3.2	1.9–5.3
T3-4; N+	8.9	0.5	0.4	0.2–0.8
M+	0.6	0.0	0.0	0.0–0.2
Unknown	12.7	0.7	0.9	0.3–2.6
P value	0.001[a]			0.0001[b]

OR, odds ratio; aOR, OR adjusted for the other factor; 95% CI, 95% confidence interval of aOR; ref, reference category; PSA level, prostate-specific antigen level.
[a] Chi-2 test.
[b] Likelihood ratio.

palpable tumours (stage T2), moderately high PSA levels and Gleason scores less than 8. Local radiotherapy of the prostate was chosen in slightly older patients, with clinical stages which were more often locally advanced (T2 N0 M0, but also T3-4 N0 M0 and any T N1 M0) and higher PSA levels, while the Gleason score was not a determining factor. Treatment by hormonal therapy alone was reserved for elderly patients with aggressive disease (high Gleason score) and advanced stages (advanced disease and metastasis, high PSA level). Watchful waiting was the preferred option in elderly patients with an early stage of disease (localised clinical stage T1 N0 M0, normal PSA level) and which had a low aggressivity (low Gleason score).

Taking into account the patient's age and stage at diagnosis, the probability of receiving one treatment rather than another was strongly related to the patient's area of residence and also to the sector of activity of the urologist who made the diagnosis (Tables 3–6 *P* value).

The probability of treatment by radical prostatectomy was three times higher in the Tarn area and almost twice as high in the Haut-Rhin region than in the other areas. It was almost 3 times higher for patients who were diagnosed in the private sector.

The same was true for the other treatments received: area of residence influenced the probability of receiving radiotherapy rather than another treatment (almost

Table 4
Variations in choice of radiation therapy (Rx) according to medical and non-medical determinants

	Univariate analysis		Multivariate analysis	
	% of Rx	OR	aOR	95% CI
Area				
Bas-Rhin[ref]	10.7	1.0	1.0	–
Calvados	34.2	4.3	5.7	3.1–10.4
Isère	16.3	1.6	2.0	1.1–3.8
Haut-Rhin	18.0	1.8	1.6	0.8–2.9
Tarn	11.7	1.1	1.1	0.6–2.1
P value	0.001[a]			0.0001[b]
Sector				
Public[ref]	19.6	1.0	1.0	–
Private	17.4	0.9	0.5	0.4–0.8
P value	0.4[a]			0.004[b]
Age (years)				
<60[ref]	13.9	1.0	1.0	–
60–69	23.3	1.9	2.3	1.0–4.9
70–79	21.4	1.7	1.9	0.9–4.1
≥80	4.6	1.0	0.3	0.1–0.9
P value	0.001[a]			0.0001[b]
PSA level (ng/dl)				
<4[ref]	12.5	1.0	1.0	–
4–9	17.8	1.5	1.6	0.6–4.1
10–19	23.8	2.2	1.9	0.7–4.7
≥20	20.3	1.8	2.0	0.8–5.0
Unknown	5.2	0.4	0.5	0.1–1.5
P value	0.001[a]			0.005[b]
Gleason score				
2–6[ref]	19.9	1.0	–	
7	16.6	0.8	–	
8–10	17.1	0.8	–	
Unknown	2.9	0.1	–	
P value	0.07[a]			
Clinical stage				
T1[ref]	11.8	1.0	1.0	–
T2	21.6	2.1	2.1	1.2–3.5
T3–4; N+	36.3	4.3	5.0	2.8–9.0
M+	3.5	0.3	0.2	0.1–0.6
Unknown	11.1	0.9	1.3	0.5–3.6
P value	0.001[a]			0.0001[b]

OR, odds ratio; aOR, OR adjusted for the other factor; 95% CI, 95% confidence interval of aOR; ref, reference category; PSA level, prostate-specific antigen level.
[a] Chi-2 test.
[b] Likelihood ratio.

6-fold higher in the Calvados area) and of receiving hormonal therapy (approximately 3–5 times lower in the Calvados and Tarn areas, respectively). The probability of not having a specific treatment was approximately 2 times lower in the Haut-Rhin area. Patients treated in the private sector had an almost 2-fold higher probability of receiving hormonal therapy, whereas the public sector favoured radiotherapy with curative intent and watchful waiting.

Clinical stage at diagnosis was not an interaction factor between non-medical determinants and the treatment choice, since the differences observed between areas and between sectors of activity persisted when radical prostatectomy and local radiotherapy were assessed only among the locally confined stages, and also when local radiotherapy and hormonal treatment alone were studied in the locally advanced stages.

4. Discussion

A preliminary investigation in four French administrative regions enabled us to define the principal characteristics of our cohort and to establish the medical factors determining the initial treatment carried out [7].

The initial treatment received by our cohort, for all disease stages, was curative in 39% of cases (surgical 21%, local radiotherapy 18%) and non-curative in

Table 5
Variations in choice of hormonal therapy (Horm) according to medical and non-medical determinants

	Univariate analysis		Multivariate analysis	
	% of Horm	OR	aOR	95% CI
Area				
Bas-Rhin[ref]	43.9	1.0	1.0	–
Calvados	26.6	0.5	0.3	0.2–0.5
Isère	41.3	0.9	0.6	0.4–1.0
Haut-Rhin	47.9	1.2	0.9	0.5–1.5
Tarn	25.4	0.4	0.2	0.1–0.4
P value	0.001[a]			0.0001[b]
Sector				
Public[ref]	40.6	1.0	1.0	–
Private	35.2	0.8	1.7	1.2–2.6
P value	0.09[a]			0.004[b]
Age (years)				
<60[ref]	19.4	1.0	1.0	–
60–69	22.2	1.2	1.3	0.6–2.9
70–79	40.1	2.8	4.3	1.9–9.8
⩾80	63.6	7.3	11.8	4.7–26.0
P value	0.001[a]			0.0001[b]
PSA level (ng/dl)				
<4[ref]	12.5	1.0	1.0	–
4–9	14.7	1.2	1.2	0.4–3.6
10–19	22.0	2.0	1.3	0.5–3.8
⩾20	57.1	9.3	3.4	1.3–9.3
Unknown	35.1	3.8	2.1	0.7–6.0
P value	0.001[a]			0.0001[b]
Gleason score				
2–6[ref]	28.6	1.0	1.0	–
7	44.9	2.0	1.8	1.2–2.9
8–10	59.2	3.6	2.3	1.4–3.8
Unknown	28.6	1.0	0.2	0.1–0.4
P value	0.001[a]			0.0001[b]
Clinical stage				
T1[ref]	15.7	1.0	1.0	–
T2	23.9	1.7	1.6	1.0–2.7
T3-4; N+	48.6	5.1	3.0	1.7–5.3
M+	84.3	28.8	28.2	14.2–55.7
Unknown	25.4	1.8	1.1	0.5–2.3
P value	0.001[a]			0.0001[b]

OR, odds ratio; aOR, OR adjusted for the other factor; 95% CI, 95% confidence interval of aOR; ref, reference category; PSA level, prostate-specific antigen level.
[a] Chi-2 test.
[b] Likelihood ratio.

61%. There are large differences from one country to another; in the United States 62% of patients have received curative treatment according to the population data of the Surveillance, Epidemiology and End Results (SEER) programme [8], whereas in Sweden less than 10% of patients have received curative treatment, and this variation could not be accounted for by differences in age or disease stage at diagnosis [9].

Our study revealed marked geographical variations. For patients of the same age and a similar disease stage and when taking into account the healthcare sector in which the diagnosis was made, the Tarn area (South-Western France) had a very high rate of radical prostatectomy, both in the private and public sectors. Calvados (North-Western France) had a high rate of radiotherapy, whereas the areas of Eastern France (Haut-Rhin and Bas-Rhin) had higher rates of hormonal therapy than the others and the Isère area (South-Eastern France) tended to prescribe radiotherapy and hormonal therapy. Tarn is a fairly rural area, where the private sector is strongly represented, there is no university hospital and urologists outnumber radiotherapists. By contrast, Calvados possesses a university hospital, a specialised cancer centre and a higher proportion of radiotherapists. Fowler showed that specialists overwhelmingly recommend the treatment that they themselves deliver [10], and the differences observed between these areas (and which were found in both the

Table 6
Variations in choice of watchful waiting (WW) according to medical and non-medical determinants

	Univariate analysis		Multivariate analysis	
	% of WW	OR	aOR	95% CI
Area				
Bas-Rhin[ref]	28.3	1.0	1.0	–
Calvados	20.1	0.6	0.7	0.4–1.3
Isère	22.5	0.7	0.8	0.5–1.5
Haut-Rhin	17.0	0.5	0.6	0.3–1.1
Tarn	26.4	0.9	1.4	0.8–2.4
P value	0.05[a]			0.08[b]
Sector				
Public[ref]	26.3	1.0	1.0	–
Private	21.0	0.7	0.4	0.3–0.7
P value	0.06[a]			0.0001[b]
Age (years)				
<60[ref]	16.7	1.0	1.0	–
60–69	18.4	1.1	1.6	0.7–3.8
70–79	24.3	1.6	3.0	1.3–6.8
⩾80	30.6	2.2	4.2	1.8–10.2
P value	0.01[a]			0.0002[b]
PSA level (ng/dl)				
<4[ref]	57.1	1.0	1.0	–
4–9	28.8	0.3	0.3	0.2–0.7
10–19	17.3	0.2	0.2	0.1–0.5
⩾20	11.8	0.1	0.2	0.1–0.4
Unknown	45.5	0.6	0.5	0.2–1.1
P value	0.001[a]			0.0001[b]
Gleason score				
2–6[ref]	29.5	1.0	1.0	–
7	7.3	0.2	0.3	0.2–0.5
8–10	11.0	0.3	0.4	0.2–0.8
Unknown	60.0	3.6	4.0	1.7–9.5
P value	0.001[a]			0.0001[b]
Clinical stage				
T1[ref]	54.6	1.0	1.0	–
T2	13.2	0.1	0.1	0.1–0.2
T3-4; N+	6.2	0.1	0.1	0.0–0.2
M+	11.6	0.1	0.1	0.1–0.2
Unknown	39.7	0.6	0.6	0.3–1.2
P value	0.001[a]			0.0001[b]

OR, odds ratio; aOR, OR adjusted for the other factor; CI, 95% confidence interval of aOR; ref, reference category; PSA level, prostate-specific antigen level.
[a] Chi-2 test
[b] Likelihood ratio

private and public sectors) may well be essentially structural, related to the distribution of the various specialties. The high frequency of hormonal therapy prescription in the region of Alsace (Haut-Rhin and Bas-Rhin) and in the Isère may be due to different local schools of thought, with treatment being initiated essentially by urologists.

These geographical variations had not previously been studied in France for prostate cancer. In Europe, only one similar study had been carried out in The Netherlands. The results from this study revealed variations from one hospital to another, depending on their size [11], but the researchers did not study regional variations. In the United States, geographical variations in treatment of radical prostatectomy, taking into consideration the disease stage and the age of the patient, were found by several authors in the SEER programme [4,12,13], certain states, such as Utah, having a much higher rate of surgery than the others. Geographical variations in the rate of treatment by local radiotherapy were also revealed in population data. Between 1992 and 1994, Mettlin found that the proportion of patients receiving radiotherapy (all disease stages, adjusted for age) ranged from 24 to 33% according to the region [14]. Lai found in non-surgical patients a geographical variation which was most marked in the 45–55 year age group and after the age of 80 years [3].

Analysis of the healthcare sector in which the diagnosis was made, taking into account age, disease stage and the area of residence, showed that in France in 1995 the private sector was strongly associated with radical prostatectomy and more frequent use of hormonal therapy. Prostate cancer is generally diagnosed by urologists, and as Fowler pointed out [10], the latter tend to favour the treatment they themselves carry out, radical prostatectomy. What is the reason behind the differences observed between the private and public sectors? One explanation is that one of the goals of private clinics is profitability and that, as their mode of operation makes prostatectomy more profitable than radiotherapy, urologists are thus better represented among them. Another possible explanation is that, in 1995, the hospitals of the public sector had set up multidisciplinary units in which urologists, radiotherapists, oncologists, pathologists and other specialists met to discuss initial treatment decisions for each individual patient. Such meetings were only just starting in the private sector, and it is possible that in the public sector they changed the therapeutic indications in some cases and decreased the influence of the urologists.

Identifying variations in practice according to non-medical determinants, such as area of residence or the sector of activity of the treating urologist, is only of value if treatment practices are consistent and 'gold standards' are agreed upon (which is not the case for prostate cancer), or if we have a reliable, final measure

of therapeutic efficacy. We can take as an example the administrative areas of Tarn and Calvados, which are fairly similar in terms of the clinical presentation of patients and tumours: in both areas, the healthcare available is largely provided by the private sector, but Calvados offers much greater possibilities for radiotherapy than Tarn, having clinics with a surgical orientation. Both areas have a similar incidence of prostate cancer, but mortality is much higher in Calvados. Interestingly, our study shows that these two areas differ greatly in the initial treatment proposed: Calvados opts for radiotherapy in most cases, whereas Tarn proposes surgery. However, at this stage of the survey, it is difficult to attribute this difference in mortality to differences in the initial treatment received alone. The administrative areas of Western France have a reputation for completing the death certificates in a much more exhaustive manner, and it is possible that the existing differences in mortality may be because prostate cancer is more often noted in Calvados. It is therefore of fundamental importance to have at our disposal a reliable measure of efficacy which will be able to determine whether the observed differences in treatment practices result in a lower chance of survival for the patient: observed survival and survival without biological recurrence should help to provide us with an answer and these data are now being collected.

Other potential determinants of the initial treatment received have been identified in American studies, but could not be verified in our study because they were not available in the medical records of the treating physicians and would require direct questioning of the patients, which was not possible in this study. These determinants include ethnic origin [3,15,16], socioeconomic status or poverty [17,18] and marital status [3,4,17–19].

5. Conclusions

We found that in France, as in other developed countries, the initial treatment of prostate cancer varies considerably according to geographical criteria and the healthcare sector.

This is the first study based on population data carried out in this country. It is now of fundamental importance to collect data on 5-year survival and recurrence rates in these patients to find out whether this disparity leads to unequal chances of survival from one area or one healthcare sector to another. While screening, organised or not, is becoming widespread in all countries, it is becoming much more important to have reliable information on later therapeutic management and its effectiveness and on the impact of developments in treatment, as well as guidelines on the evolution in treatment practices. Investigations such as

our study, if carried out regularly, will allow us to assess the importance of changes in practice patterns. With this aim in mind, we are setting up a representative cohort of prostate cancers diagnosed in France in 2002 which will make comparison possible.

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