Prostate Cancer Survivorship in Switzerland (PROCAS): Study Protocol of the Swiss Multiregional Cohort

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PROCAS

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Introduction

In 2018, 1.276 men were assumed to be diagnosed with prostate cancer (PC) worldwide and around 6,800 in Switzerland [1]. PC prognosis has substantially improved during the past decades, leading to five-year relative survival rates of 90% to 95% in developed countries (Switzerland 90%) [2-4]. Consequently, the number of men being alive five years after initial diagnosis of PC (long-term survivors [5]) has substantially increased [6]. For Switzerland it was projected that in 2015 around 32,818 men will be PC long-term survivors. This number has tripled since 2000 [7]. As the number of long-term PC survivors continues to increase, it is important to assess and understand cancer survivorship aspects, such as health-related quality of life (HRQoL) and symptom burden [8, 9].

So far, studies assessing HRQoL in long-term PC survivors, reported that long-term PC survivors have generally good HRQoL, which is relatively comparable to that of population controls [10]. However, PC survivors do experience detriments in specific aspects of HRQoL (e.g. social, role, emotional and physical function), higher symptom burden for example in fatigue, diarrhoea, erectile dysfunction and urinary problems as well as higher depression and anxiety rates [11-13]. Moreover, HRQoL and well-being are influenced by several factors such as clinical and demographic characteristics [14]. Treatment can also represent a crucial factor in explaining HRQoL differences among cancer patients [11, 13]. Therefore, information on HRQoL has the potential to support treatment decision-making and post-treatment health care for survivors and health care providers [15, 16].

So far, research regarding HRQoL, symptoms and psychological well-being in long-term PC survivors is relying on data mostly from the US and to a small extent from Scandinavian countries, the Netherlands, the UK and Germany [11, 13, 17]. Differences in health care administration including follow-up of PC survivors and rehabilitation may limit the generalizability of the current knowledge regarding HRQoL, symptoms and psychological well-being in long-term PC survivors. The Prostate Cancer Survivorship in Switzerland (PROCAS) project aimed at filling the gap in existing knowledge about HRQoL, symptoms as well as disease and treatment-related late effects of long-term PC survivors in Switzerland.

Study Objectives

The overall aim of the PROCAS study was to provide knowledge on HRQoL, symptoms as well as disease and treatment-related late effects in long-term PC survivors for patients, health care professionals and caregivers.

In detail, we defined as our primary objective to describe HRQoL in long-term PC survivors in Switzerland depending on personal and medical factors, such as: age, tumour stage, language group, treatment, socioeconomic status and comorbidities. In our secondary objective we aimed to identify determinants for negative and positive effects on HRQoL.

Study Design and Inclusion Criteria

PROCAS is a multiregional cohort study with prospective collection of information about HRQoL, symptoms, psychological well-being, personal and medical data of long-term PC survivors. The study was developed in close cooperation with involved Swiss cancer registries, the Swiss

Fig. 1. PROCAS Study Regions. RFT - Registre Fribourgeois des Tumeurs, KRBB - Krebsresgister beider Basel, KSGR - Krebsregister Graubünden und Glarus, KROCH Krebsregister Ostschweiz, RVST - Registre Valaisan des Tumeurs & KRZHZG - Krebsregister der Kantone Zürich und Zug.

Society of Urology and the Swiss Patient Organisation for Urological Diseases. The National Institute of Cancer Epidemiology and Registration (NICER) was the central study centre for this study. Six cancer registries (Registre Fribourgeois des Tumeurs (RFT), Krebsresgister beider Basel (KRBB), Krebsregister Graubünden und Glarus (KSGR), Krebsregister Ostschweiz (KROCH), Registre Valaisan des Tumeur (RVST) & Krebsregister der Kantone Zürich und Zug (KRZHZG)) were involved as regional study centres (**Fig.** 1). This selection was a result of an open call to all ten cancer registries that were established prior to 2006.

Totally, 8,712 PC survivors fulfilled the inclusion criteria, which were:

- Male subjects
- Diagnosed with prostate cancer (ICD-10 C61) between 1th January 2006 and 31th December 2011
- Registered by one of the following cancer registries: RFT, KRBB, KSGR, KROCH, RVST & KRZHZG
- Age at diagnosis between 25 and 75 years
- Alive at time of enrolment
- Able to complete the questionnaire (assistance is possible)
- Able to understand German, French or Italian
- No concurrent bladder cancer

Data Collection and Measurements

In a first step, all urological hospital clinics and established urologists in the participating cantons were invited to participate in the study. Secondly, regional study centres drew random subsamples of patients who had been referred by the participating urologists from their registries or from patients who participated in the Patterns of Care study [18]. 1,246 participants were then invited to participate in the study by their referring urologist by postal mail (**Fig.** 2). Out of these, 1,194 could finally be contacted and received an invitation letter, the patient questionnaires (A) and informed consent by postal mail between February 2017 and March 2018. Totally, 748 participants

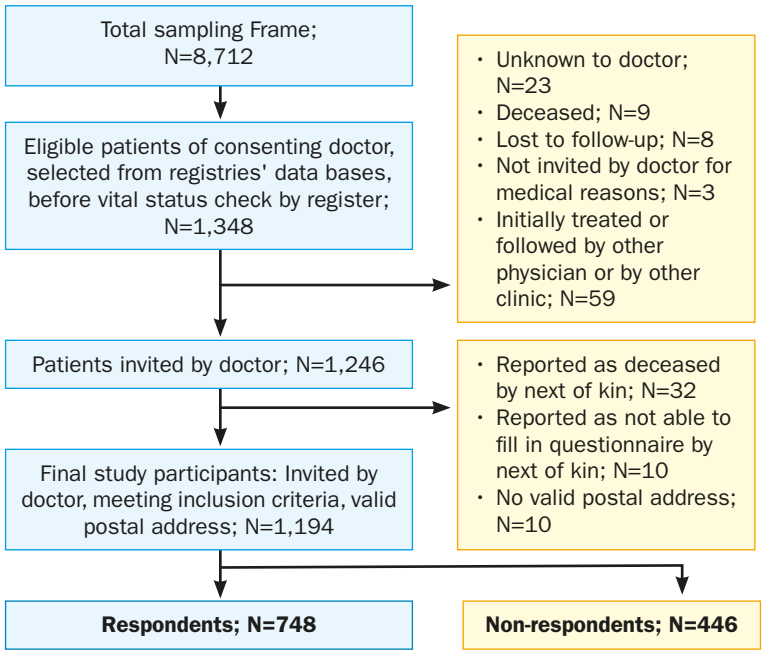

Fig. 2. Recruitment of Prostate Cancer Survivors.

responded (Response Rate: 62.6%) and sent back the documents. Non-responders received one reminder. In case of questions, participants could phone the central study center. After receiving the documents from the patients, regional study centres asked the referring physician to provide additional medical data via a short physicians' questionnaire (B). All documents were available in German, French and Italian.

After the recruitment of patients for this project, regional study centres prepared a coded patient data extract (C) of all patients fulfilling the inclusion criteria for the PROCAS project. The data extract included status of participation (respondents, non-respondents & not-invited) and clinical information.

Clinical Data

Data regarding initial tumour stage, year of birth and year of initial diagnosis was obtained from the data extract (C) from the participating cancer registry.

More detailed information on treatment, relapse/disease progression and other primary tumours were gathered via the physicians' questionnaire (B). Participating survivors were also asked information in the patient questionnaire (A) about their treatment, recurrence/disease progression and other primary tumours to supplement the information from the urologists and cancer registries. Moreover, participants gave information about their comorbidities.

Sociodemographic Data

Information on age, nationality, marital status, education, occupation and Body-Mass-Index were provided by the patients (A).

HRQoL, Symptoms and Psychological Well-being Data

All instruments used in the patient questionnaire (A) to assess HRQoL, symptoms and psychological well-being have sound psychometric properties and are validated in German, French and Italian. This allows us to compare our results with results from other studies.

The following questionnaires were used:

- HRQoL was assed using the EORTC QLQ-C30 questionnaire [19].
- PC-specific symptom burden was assessed using the EORTC QLQ-PR25 questionnaire and specific items of the EPIC-26 [20,21].
- Fatigue was assessed using the EORTC QLQ-FA12 [22].
- The Mental Health Inventory (MHI) -5 was used to asses mental health [23].
- To measure spiritual well-being the FACIT-sp questionnaire was used [24].

Ethical Aspects

The study has been approved as a multi-centre study by the Ethics Committee Zurich and by all review boards accountable for the participating cancer registries (BASEC Number: 2016-00608). All participants were asked to provide written informed consent.

Results

The mean age of respondents at data collection was 73.2 years and mean time since diagnosis was 7.6 years (range: 5-10 years) (**Tab. 1**). Most study participants were of Swiss nationality and were living with their partner. Non-respondents and eligible PC survivors, who had not been invited, were significantly older, were less likely to be Swiss and to live together with their partners. There were no significant differences regarding disease extension.

The most common school degree among participants was a secondary school degree (43.1%) and most participants were retired (85.7%). In total, 22.3% had experienced disease progression and/or relapse and 6.6% reported a second primary cancer. The most common primary therapy was radical prostatectomy (67.0%), followed by external-beam radiation therapy (21.5%) and hormonotherapy (16.6%). Finally, the most common self-reported comorbidities were arthritis/rheumatism/arthroses (23.4%), visual impairment (17.9%), degenerative disc disease (17.5%) and hearing loss (14.4%).

Discussion

This is the first study in Switzerland in which population-based cantonal cancer registries contributed to the recruitment of cancer survivors, in this case long-term PC survivors. Therefore, the PROCAS study will allow us to assess HRQoL, well-being and symptom burden from a representative sample of long-term PC survivors. Through the multiregional approach, including patient recruitment via six population-based cancer registries located in the German and French speaking region, PROCAS represents a sociodemographically diverse cohort with patients not exclusively treated at large hospitals. Moreover, the good sample size together with the variety of validated instruments and clinical and sociodemographic data, will allow us to perform a variety of analyses to get an in-depth understanding of HRQoL, well-being and symptom burden of long-term PC survivors. Finally, the PROCAS study

Tab. 1. Demographic and clinical characteristics of respondents, non-respondents and not-invited PC survivors.

		Respondents Col%	Non-Respondents Col%	Not-Invited Col%	Respondents vs. Non-Respondents p-value	Respondents vs. Not-Invited p-value
Cancer Registry Data	Total (N)	(748)	(446)	(7,518)		
	Age at survey					
	<70 years	25.8	22.9	22.6		
	70-74 years	13.6	25.8	27.0	**0.035**	**<0.001**
	75-79 years	25.1	32.3	28.7		
	>79 years	17.5	19.1	21.5		
	Mean (SD)	73.2 (6.4)	74.0 (6.2)	74.0 (6.4)	**0.035**	**0.002**
	Time since diagnosis					
	5-6	27.3	25.8	31.9		
	7-8	42.0	41.3	36.7	0.32	0.053
	9-10	30.7	32.9	31.4		
	Mean (SD)	7.6 (1.5)	7.7 (1.5)	8.0 (1.6)	0.32	0.053
	Nationality					
	Swiss	90.4	81.6	81.2		
	Non-Swiss	4.5	12.3	9.1	**0.001**	**0.001**
	Unknown	5.1	6.1	9.7		
	Living with partner					
	Yes	71.1	62.7	65.5		
	No	18.9	19.5	16.0	**0.007**	**0.003**
	Unknown	10.0	17.8	18.5		
	Extension of disease					
	Local	78.6	76.7	76.7		
	Regional	15.1	16.4	13.0	0.410	0.074
	Distant	5.2	4.0	3.8		
	Unknown	1.1	2.9	6.5		
	Cancer Stage					
	I	13.9	21.5	18.5		
	II	56.6	46.6	46.1		
	III	17.0	17.7	14.4	0.34	**0.045**
	IV	6.0	5.2	4.7		
	Unknown	6.6	9.0	16.3		
Questionnaire Data	Education (highest degree)[1]					
	Primary school or no degree	1.5	–	–	–	–
	Secondary	53.1	–	–	–	–
	Tertiary	44.4	–	–	–	–
	Unknown	1.1	–	–	–	–
	Employment at survey					
	Full-time	7.6	–	–	–	–
	Part-time	2.8	–	–	–	–
	(Early) Retirement	85.7	–	–	–	–
	Invalidity Insurance	2.7	–	–	–	–
	Other	0.9	–	–	–	–
	Unknown	0.3	–	–	–	–
	Disease progression/relapse (yes)	22.3	–	–	–	–
	Unknown	1.2	–	–	–	–
	Second primary cancer after PC (yes)	6.6	–	–	–	–
	Unknown	0.5	–	–	–	–
	Comorbidities (self-report)					
	Arthritis/Rheumatism/Arthroses	23.4	–	–	–	–
	Visual Impairment	17.9	–	–	–	–
	Degenerative Disc Disease	17.5	–	–	–	–
	Hearing Loss	14.4	–	–	–	–
	Primary Therapy					
	Radical Prostatectomy	67.0	–	–	–	–
	External Beam Radiation Therapy	21.5	–	–	–	–
	Brachytherapy	4.6	–	–	–	–
	Androgen Deprivation Therapy	16.6	–	–	–	–
	Watchful Waiting/Active Surveillance	6.4	–	–	–	–

[1] Education: Low (no or primary school); Medium (lower general secondary education or vocational training); High (pre-university education, high vocational training, university).

supplements data of HRQoL, well-being and symptom burden of the large group of PC survivors who are living in Switzerland and are still alive.

However, some limitations have to be considered when analysing the data. Despite the good response rate of 62.6%, there is a possibility of healthy survivor bias. Additionally, due to lack of baseline HRQoL data, we cannot adjust for baseline HRQoL. Moreover, even though we have a range of demographic and clinical data, we do not have all information on factors related to treatment (e.g. on digital rectal exam results, PSA-values, Gleason scores). Additionally, for data protection reasons, direct contact to patients via cancer registries is not possible, leading to a selection bias as not all urologists were willing to participate in the study.

Nevertheless, the study will assist researchers, survivors, caregivers and health care professionals in understanding the potential impact of PC treatments on HRQoL as well as get information on the symptom burden patterns in long-term survivors by treatment, stage, age and/or social demographic factors.

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For additional information on the PROCAS study, see the PROCAS website at *http://www.procas.ch/*

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