Identifying Patients with Metastatic Castration-Resistant Prostate Cancers (mCRPC) in the SNDS database: CAMERRA study

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Abstract

Introduction: Management of mCRPC has evolved significantly since 2011. SNDS is the nationwide healthcare insurance system database covering 99% of the French population. In the absence of a direct marker, the identification of mCRPC patients within the SNDS database relies on the construction of a complex algorithm. ***Objective:*** To identify prevalent mCRPC patients in the SNDS database in 2014. ***Methods:*** An algorithm for identifying mCRPC patients was build from an extraction of men over 40 years old with an indicator of prostate cancer (Long-term disease and diagnosis codes according to the Interna-tional Classification of Diseases [ICD 10], hospitalizations and procedures, treatments) and having a 5-years healthcare history without any gap > 1 year. The identification of mCRPC patients depends on two indicators: 1) the date of first management of metastases based on specific acts (radiotherapy, hospitalizations notably for chemotherapy, treatments targeting metastases (denosumab, zoledronic acid, radioisotopes, radiofrequencies, etc.), or drugs specific to mCRPC (abiraterone acetate, enzalutamide, docetaxel and cabazitaxel) associated with imaging procedures; 2) the date of castration resistance based on switch between sequences of anti-androgens and LH-RH analogs, surgical procedures (orchiectomy and pulpectomy), or first dispensing of specific treatments for mCRPC following imaging procedures. A patient was identified as having mCRPC when a date of first management of metastases and a date of castration resistance were identified in his history. ***Results:*** 3 192 patients with prevalent prostate cancer in 2014 were identified in the 1/97th sample of the SNDS database (EGB), including 499 metastatic and 254 castration-resistant. Of these 3 192 patients, 141 were identified as having a mCRPC in 2014. By extrapolation, 468 142 prevalent prostate cancer patients are expected in the SNDS database in 2014. This estimate concurs with that one of the French National Cancer Institute, 508 699 in 2008. Among these prevalent prostate cancers, 20 719 should be a mCRPC. ***Conclusion:*** Considering results of this preliminary study, a functional algorithm for identifying mCRPC patients has been constructed according to complex elements and their sequences, giving rise to a first estimate of its prevalence in the French population from the SNDS.

Background

- **Prostate cancer**
  - Most common cancer in men, with more than 53 900 new cases in 2011 in France*
  - Slow but unavoidable disease progression to metastatic and/or castration-resistant stage
- **Major changes in metastatic castration-resistant prostate cancer (mCRPC) management**
  - In 2012 and 2013, abiraterone acetate and enzalutamide obtained respectively a European marketing authorization for the treatment of mCRPC patients previously treated by docetaxel
  - High potential changes in mCRPC patients care pathway
- **CAMERRA study**
  - Aims to assess the therapeutic strategic changes for mCRPC between 2012 and 2014 from data of the French nationwide claims and hospital database (SNDS)
  - However, no direct markers are available to identify mCRPC in the database

Objective: to design an algorithm for mCRPC identification in the SNDS in 2014

**Source INCa: Cancers in France, 2016 edition, National Cancer Institute, April 2017*

Methods

- **Data source**: EGB (*Echantillon Généraliste des Bénéficiaires*)
  - 1/97th representative sample of SNDS, which covers 99% of the French population (66.6 million people)
  - Includes individual anonymous information on reimbursed outpatients claims, national hospital-discharge summaries, and national death registry
- **Study period:** 01/01/2009 to 12/31/2014
- **4 steps to identify prevalent mCRPC cases**
  - **Step 1 = Identification of prostate cancer**

    Inclusion criteria
    - Men ≥ 40 years old and alive on 01/01/2014, covered by the national health insurance "*Régime Général*" without any gap > 1 year in their 5-year healthcare history
    - With a prostate cancer indicator:
      i. Long-term disease registration (LTD) for prostate cancer (ICD10 = C61)
      ii. Hospital stay in 2014 with a diagnosis of prostate cancer (C61 as primary, related or associated diagnosis), and a prostate cancer specific treatment between 2009 and 2014 (radical prostatectomy, brachytherapy, hormonotherapy, *etc.*)
      iii. Dispensing in 2014 of prostate cancer specific treatment: androgen deprivation therapy (GnRH analogs/antagonists or antiandrogens), new generation hormonotherapy (e.g. abiraterone, enzalutamide), estramustine, or chemotherapy

    Exclusion criteria
    - Patients without LTD registration or hospitalization for prostate cancer and having:
      i. LTD registration for persistent delusional disorders (F22), specific personality disorders (F60), unspecified mental retardation (F79), or gender identity disorders (F64)
      ii. Androgen deprivation therapy with less than 3 PSA tests
  - **Step 2 = Identification of metastatic cases**

    Date of first metastases management based on specific drug or procedures:
    - Radiotherapy session for metastases
    - Hospital stay with "secondary malignant neoplasm" as diagnosis (ICD10 = C77, C78, C79) associated with a LTD or a diagnostic code for prostate cancer
    - Dispensing of bone metastases targeted therapy: denosumab, zoledronic acid, hepatic radiofrequency ablation, beta particle emitting radionuclides (e.g. strontium-89, samarium-153, radium-223)
    - Initiation of a GnRH analog within 2 months of prostate cancer diagnosis in young patient (< 70 years old) without any local prostate cancer treatment prior
    - Initiation of a specific mCRPC treatment if preceded by at least 3 months of continuous androgen deprivation therapy and within 4 months after a specified medical imaging procedure
  - **Step 3 = Identification of castration-resistant cases**

    Date of castration-resistance relying on:
    - Switches between androgen deprivation therapy treatments (anti-androgen, GnRH analog/antagonist)
    - Surgical castration (orchiectomy or testicular pulpectomy)
    - Initiation of estramustine or mCRPC specific treatment
  - **Step 4 = Identification of mCRPC cases**

    Patients were considered as mCRPC when a date of first metastases management and a date of castration-resistance were identified in their medical history (Figure 1)

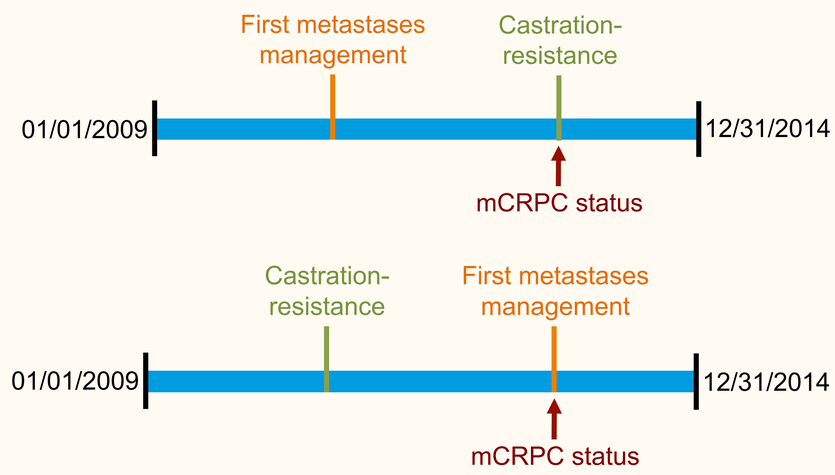

Figure 1. Chronology between first metastases management, castration-resistance and mCRPC status

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Declaration of interest: The CAMERRA study is carried out by the Bordeaux PharmacoEpi platform in collaboration with Janssen® company and supervised by a Scientific Committee.

Results

- **Identification of prevalent mCRPC cases in 2014 (Figure 2.)**
  - A total of 3 192 patients with a prostate cancer were identified in the EGB in 2014. By extrapolation, around 468 100 prostate cancers are expected in the SNDS in 2014
  - Among the 3 192 prevalent cases of prostate cancer identified, 273 had metastases and 187 were castration-resistant. Thus, 111 patients were classified as mCRPC in the EGB. By extrapolation, around 16 300 mCRPC cases are expected in the SNDS in 2014

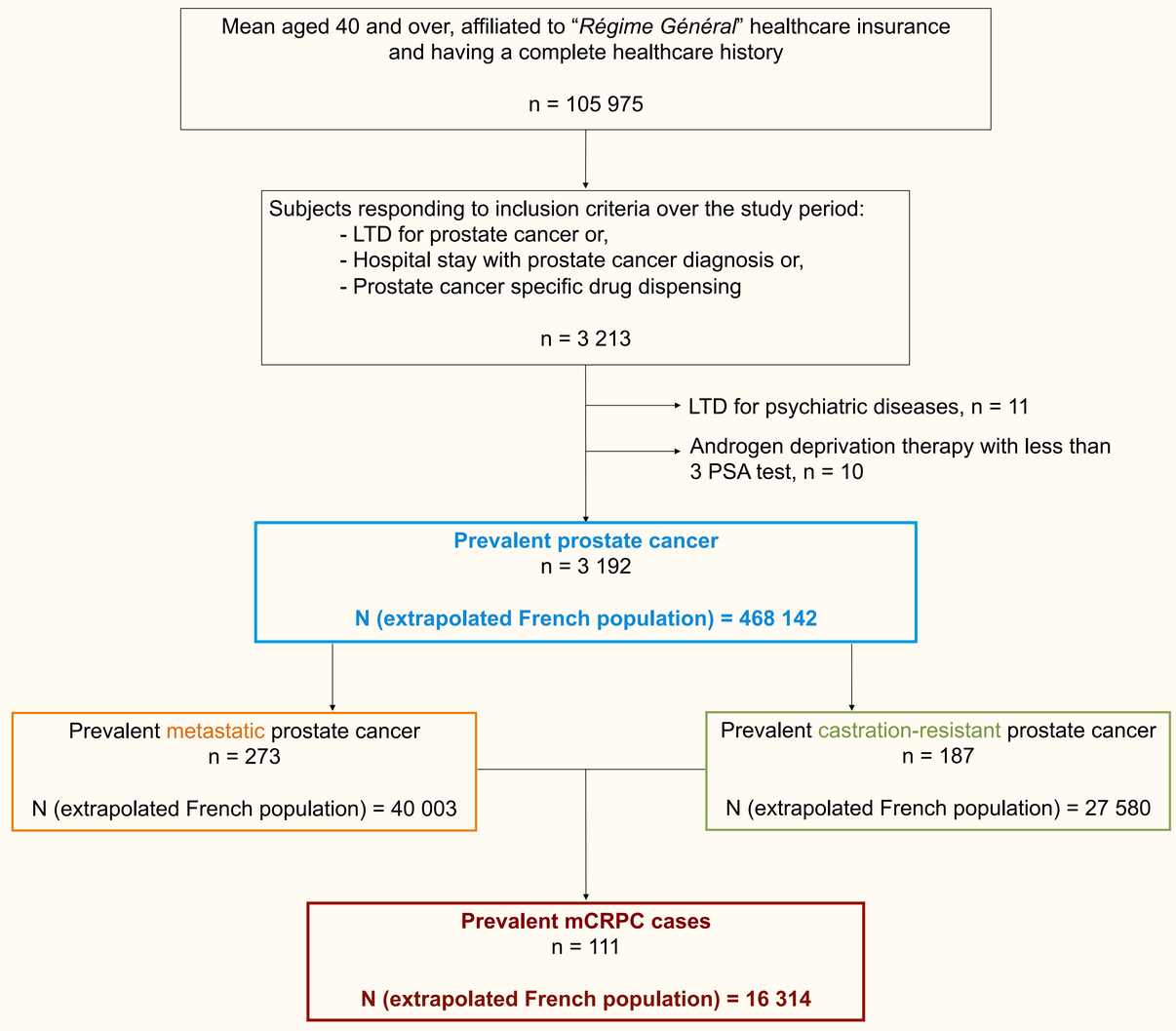

Figure 2 : Flowchart for identification of prevalent mCRPC cases in 2014 from EGB database

- **Identification parameters of mCRPC patients in 2014**

✓ **Metastases (Table 1.)**

- Radiotherapy is the main indicator of metastases among patients with prostate cancer
- The date of first metastases management for mCRPC patients corresponds mainly to diagnostic codes of secondary tumors consecutive to a hospital stay (36%), and to the initiation of a specific mCRPC treatment following an imaging procedure (30%)

Table 1. Indicators to identify the date of 1st metastases management for patients with prostate cancer and for patients with mCRPC in the EGB in 2014

	Prostate cancer n = 3 192		mCRPC n = 111	
Radiotherapy session for metastases, n (%)	98	(3.1)	10	(9.0)
Diagnosis of secondary tumor consecutive to a hospitalization or a LTD registration for prostate cancer, n (%)	85	(2.7)	40	(36.0)
Dispensing of bone metastases targeted treatments: denosumab or zoledronic acid, n (%)	43	(1.3)	16	(14.4)
Targeted beta or alpha particle therapy for bone metastases, n (%)	1	(0.0)	1	(0.9)
Initiation of a mCRPC specific treatment following 3 months of androgen deprivation therapy and a specified imaging procedure, n (%)	33	(1.0)	33	(29.7)
Initiation of a GnRH analog within 2 months of the prostate cancer diagnosis in young patient without any local treatment prior, n (%)	13	(0.4)	11	(9.9)
Radiofrequency ablation of liver metastases, n (%)	0	(0.0)	0	(0.0)

✓ **Resistance (Table 2.)**

- Switches between androgen deprivation therapy treatments (introduction or discontinuation of anti-androgens) are the main indicator of castration-resistance among patients with prostate cancer
- The date of castration-resistance for mCRPC patient relies mainly on the initiation of a specific CRPC or mCRPC treatment (56%) and the switches between androgen deprivation therapy treatments (44%)

Table 2. Indicators to identify the date of castration resistance for patients with prostate cancer and for patients with mCRPC in the EGB in 2014

	Cancer prostate n = 3 192		mCRPC n = 111	
Initiation of a CRPC or mCRPC specific treatment, n (%)	70	(2.2)	62	(55.9)
Introduction for ≥ 2 months of an anti-androgen after a 3 months period with an GnRH analog or antagonist, n (%)	70	(2.2)	30	(27.0)
Discontinuation for ≥ 2 months of an anti-androgen after 3 months of total androgen blockade**, n (%)	47	(1.5)	19	(17.1)
Orchiectomy or testicular pulpectomy after 3 months of androgen deprivation therapy, n (%)	0	(0.0)	0	(0.0)

***provided that cancer is not in remission of disease*

Conclusion

- Preliminary study that has allowed the construction of a **functional algorithm for identifying mCRPC patients** according to complex elements and their sequences
- **Prevalence estimates from EGB in France in 2014** are consistent with the National Cancer Institute (INCa)
  - Expected number of **prostate cancers: 468 100** (508 700 in 2008, INCa)
  - Expected number of **mCRPC: 16 300**
- This algorithm will be assessed through a validation study and applied to SNDS to obtain the actual prevalence of prostate cancer and mCRPC in the overall French population

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