



Prostate Cancer in Deceased Organ Donors: Loss of Organ or Transplantation With Active Surveillance

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ABSTRACT

Introduction. Prostate cancer has become an important clinical issue within deceased organ donors. There is still a considerable number of undiagnosed cancers, especially in early stage, despite frozen section analysis. The aim of the study was to evaluate outcomes of orthotopic liver transplants (OLTx) with organs from donors with prostate cancer.

Material and Methods. A retrospective analysis was performed in deceased liver donors whose prostate glands were harvested for histologic examinations because of prostate cancer suspicion. The study group consisted of 72 men reported as potential liver donors between 2011 and November 2017. Prostate glands were primarily assessed by frozen sections and afterward in routine examination. Generally cancer diagnosed in frozen specimen was not considered for OLTx. Recipients who received an organ from the donor with prostate cancer were actively surveilled.

Results. There were 19 cases (26.40%) of prostate cancer diagnosed among the study group. In 12 cases diagnosis was made by frozen section assessment, of which 11 organs were disqualified from OLTx and 1 was transplanted. In 7 cases prostate cancer was diagnosed after OLTx in final routine histologic examination. Finally, 8 recipients (5 men and 3 women) received a new organ. Only 1 died during the perioperative period. In the remaining 7 patients the perioperative period was uneventful and no disease transmission was observed during follow-up.

Conclusions. Diagnosis of prostate cancer in donors should not be treated as a contraindication for OLTx because the risk of disease transmission is low. Potential recipients must be fully informed and kept under oncological surveillance.

WORLDWIDE, there has been an annual increased incidence of prostate cancer (approximately 1,600,000 new cases) and 366,000 prostate cancer deaths, making it the most commonly diagnosed cancer in men and the seventh leading cause of male cancer death [1,2]. Serum prostate-specific antigen (PSA) is the most frequently used screening test for prostatic cancer diagnosis [3]. However, there are several causes of elevated PSA concentration, which may lead to overdiagnosis [4]. This tendency can also be noticed among deceased organ donors, but there is still no widely accepted diagnostic algorithm in cases of prostate cancer suspicion in potential organ donors. It is essential to continue making progress in that field as perioperative histologic examination of prostate frozen sections has relatively low sensitivity, especially in patients with early-stage

prostate cancer. Final diagnosis is made by routine histologic examination; the result is available after at least 7 days posttransplant.

The aim of this study was to evaluate outcomes of orthotopic liver transplant (OLTx) in patients with acute and chronic liver insufficiency who received organs from donors diagnosed with prostate cancer after final histologic examination. Authors have also reviewed available research papers and international societies' recommendations on use

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of organs harvested from donors diagnosed with malignant neoplasms.

MATERIAL AND METHODS

We retrospectively analyzed 72 cases in which transplanted organs were derived from donors whose prostate glands were histologically examined because of elevated PSA level (>10 ng/dL) and abnormal digital rectal examination. Intraoperatively diagnosed pelvic lymph node enlargement was another indication for histologic examination of prostate glands. Examination was first performed on frozen sections. Final diagnoses were made after 7 days by routine histologic examinations. All OLTx were performed in the Department of General, Transplant and Liver Surgery at the Medical University of Warsaw between 2011 and November 2017.

RESULTS

Among all examined prostate glands ($n = 72$) there were 19 cases (26.40%) of cancer. Twelve were previously diagnosed during examination of frozen specimens and confirmed during final examination. Eleven livers derived from these donors were disqualified from OLTx and 1 was transplanted after risk acceptance and receipt of formal consent from the recipient. In the remaining 7 cases harvested livers were transplanted because of positive results of frozen section analyses, and prostate cancers were diagnosed only after final histologic examination. In all 8 of these cases in which liver was derived from the donors with malignant prostate neoplasms, tumor was identified as low-grade carcinoma (Gleason 3 + 3). Among them there were 7 donors with single tumor focus identified with mean diameter of 2.5 mm (range, 1–8 mm) and only 1 prostate gland with 2 foci (both 3 mm in diameter). Median age of these donors was 63 years and serum PSA concentration was 12 ng/dL. In donors whose livers were not transplanted, prostate tumors were identified in 6 patients as Gleason (3 + 3) with mean diameter 3.3 mm (2 with single focus, 3 with double foci, and 1 with hexuple foci) and in 5 patients as Gleason (4 + 3 or 3 + 4). Median age of these donors was 62 years ($P = .95$) and median serum PSA concentration (16 ng/dL) was not significantly higher than in the previous group ($P = .95$).

Table 1. Comparison of Donors and Tumor Characteristics

Donor Variable	Donors of Used Organs $n = 8$	Donors of Unused Organs $n = 11$	P Value
Age, median (range), y	63 (58–65)	62 (44–69)	NS
PSA serum concentration, median (range), ng/dL	12 (2.71–67.0)	16 (7.70–55.30)	NS
Cancer Advancement			
Gleason ≤ 6	8 (100%)	6 (54.5%)	NS
Gleason > 6	0 (0%)	5 (45.5%)	<.05
Single focus	7 (87.5%)	3 (27.3%)	<.05
Multifocal	1 (12.5%)	8 (72.7%)	<.05
Gland margin infiltration	0	2	NS

Abbreviations: NS, not significant; PSA, serum prostate-specific antigen.

Recipient group ($n = 8$) consisted of 5 men and 3 women. Median age was 57 years. Indications for OLTx were acute liver failure due to *Amanita phalloides* poisoning (1), alveolar echinococcosis (1), primary biliary cirrhosis (1), hepatocellular carcinoma (2), alcoholic liver disease (2), and cryptogenic cirrhosis (1). All recipients had been informed about donors' malignant prostate neoplasms and put on precise oncologic surveillance (physical examination, abdominal USG, and chest X-ray). Donor and recipient characteristics are shown in Table 1. The recipient that qualified for emergency OLTx because of mushroom poisoning died in the perioperative period due to multi-organ failure. No disease transmission was observed during follow-up (median, 6 months; range, 2–24 months). Overall survival rate (Kaplan-Meier method) was 87.5% after 2 years.

DISCUSSION

Prostate cancer among donors raises serious clinical and decision-making issues. On the one hand, we are facing organ shortage; on the other hand, expanding the donor pool to patients with malignant disease raises concerns about disease transmission. Up to now, it was necessary to exclude the presence of prostate and any other carcinoma in donors before transplant of harvested organs. However, normal concentration of PSA in donors cannot justify the exclusion of prostate cancer; the representative observational study by Thompson et al showed that 21% of men with PSA <3.0 ng/dL were diagnosed as having prostate cancer by their 7-year follow-up [5]. Focal prostate cancer has also been found incidentally among patients after radical cystoprostatectomy because of bladder cancer [6]. More than 50 years ago autopsy studies reported prostate cancer incidence at 30% among men older than 50 years [7]. According to these studies it can be assumed that similar correlations can be observed among the population of deceased donors. It is crucial to select men with latent prostate cancer who have higher risk of progression. According to the National Comprehensive Cancer Network [8], prostate cancer confined to the gland is considered a low-risk tumor (Gleason 3 + 3 and PSA < 10 mg/dL). In this particular group patients do not require radical surgery and remain under active surveillance (PSA level, digital rectal examination, and needle biopsy) [9].

Prostate cancer is not diagnosed in every donor with elevated PSA concentration >4 ng/dL, therefore, OLTx should be continued [10,11]. Frozen section examination is not routinely used for prostate cancer diagnosis and its feasibility in assessment of tumor margins after radical prostatectomy is not well defined [12]. Random needle biopsy could be falsely negative in cases where tumor is not microscopically visible. The prostate gland can be fully evaluated only during routine histologic examination. However, the decision about using the harvested organ, which is limited by cold ischemia time, has to be made upon assessment of prostate frozen specimens and, as a

consequence, there would be a considerable group of patients with organs from donors diagnosed as having prostate cancer.

Therefore, it seems crucial to create a diagnostic and management scheme for donors with early-stage prostate cancer. D'Errico-Grigioni et al recommend histologic examination in donors older than 50 years with PSA concentration >10 ng/dL, urine catheterization <5 days, and abnormal digital rectal examination or transrectal ultrasonography [13]. Use of an organ harvested from a donor with good-prognosis prostate cancer (Gleason \leq 5 or Gleason 3 + 3) is defined as standard-risk OLTx. A tumor-free gland margin is mandatory. According to recommendations of the Polish Transplantation Society Working Group, donors with prostate cancer (Gleason \leq 3 + 3) are considered donors with nonstandard risk. It is permitted to transplant such organs in life-threatening cases after careful benefit-to-risk assessment and receipt of formal consent from the potential recipient [14].

As a leading liver transplantation center in Poland, our department expands the organ donor pool to donors with early-stage prostate cancer. Furthermore, in patients with acute or acute-on-chronic liver failure, this kind of approach is strongly advised as early outcomes are promising. However, recipients of such organs should be kept under strict medical surveillance.

CONCLUSIONS

1. Number of prostate cancer cases will systematically grow due to extending donor organ age.
2. Diagnosis of prostate cancer in potential organ donors cannot disqualify them from transplantation.
3. Deceased donor pool can be extended to patients with early-stage prostate cancer.

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