Clinical outcome of surgical management for symptomatic metastatic spinal cord compression from prostate cancer

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Abstract

Background

Metastatic spinal cord compression (MSCC) from prostate cancer (PC) influence to not only prognosis but also quality of life of patients. However little were known about clinical outcome of surgery for MSCC from PC. We evaluated both oncological and functional outcome of decompression and reconstruction surgery for patients with symptomatic MSCC from PC.

Methods

We assessed 19 patients who were performed decompression and reconstruction surgery for symptomatic MSCC from PC. Those of 19 patients, 8 were patients with metastatic hormone naïve prostate cancer (mHNPC) and 11 were patients with metastatic castration-resistant prostate cancer (mCRPC).

Results

Median age of MSCC of patients with mHNPC and mCRPC were 72 and 65, respectively. Median prostate-specific antigen (PSA) levels at diagnosed as MSCC of patients with mHNPC and mCRPC were 910 ng/mL and 67 ng/mL, respectively. Although 2 out of 8 patients (25.0 %) with mHNPC were ambulatory preoperatively, 6 patients (75.0 %) were ambulatory postoperatively. Among 11 patients with mCRPC, only 3 patients (27.3 %) were ambulatory preoperatively, 6 patients (54.5 %) were ambulatory postoperatively. Median postoperative overall survival among men with mHNPC and mCPRC were not reached and 8 months, respectively.

Conclusions

Our current study demonstrated that decompression and reconstruction surgery for symptomatic MSCC form PC might contribute favorable functional outcome among men with mHNCP and mCRPC. However, its role for improving the oncological outcome remains unclear. Anyway, treatment strategy should be made by shared-decision making among patients, urologists, radiation oncologists, and orthopedic surgeons.

Background

Prostate cancer (PC) incidence has increased in worldwide [1]. Prostate-specific antigen (PSA)
screening contribute to prostate cancer mortality improvement [2], however, PC is leading cause of mortality and morbidity in globally [1]. Metastatic hormone-naïve prostate cancer (mHNPC) is an androgen dependent status and androgen ablation therapy is effective initially, however, most patients with mHNPC have been resistant to androgen ablation therapy and failed to metastatic castration-resistant prostate cancer (mCRPC) [3]. Osseous metastases are common both in patients with mHNPC and mCRPC [4, 5] and impair the quality of life from skeletal related events. Roughly one third of PC metastases to the spine become symptomatic, metastatic spinal cord compression (MSCC) [6] or mechanical instability [7]. MSCC occurred in 5 % of patients who die of cancer [8] and, influence to unfavorable prognosis and quality of life. MSCC could be cause of irreversible neurological impairment and short prognosis, therefore, treatment strategy for MSCC is important for not only living longer but also living better among men with mHNPC and mCPRC [9].

Decompression surgery is one of the standard of care for symptomatic MSCC from various cancer including PC[10]. However, clinical outcome of surgery for MSCC from PC were not fully described because of limited number of patients. In this study, we evaluated the oncological and functional outcome of decompression and reconstruction surgery for MSCC from PC.

**Methods**

**Patients**

We retrospectively assessed 19 patients who were performed decompression and reconstruction surgery for symptomatic MSCC from PC from 2002 to 2017 in Yokohama City University Medical Center and Yokohama City University Hospital. Indication for surgery was determined by multidisciplinary team management (shared decision making among patients, urologists, orthopedic surgeons and radiation oncologist) under the consideration of patient’s prognosis, neurological deficits, and overall health status. In general, patients with prognosis < 1 year and fixed neurological deficits have not been recommended for surgery. Before surgery for MSCC, all patients received high dose dexamethasone as initial treatment for prevent irreversible neurological impairment. Those of 19 patients, 8 were patients with mHNPC and 11 were patients with mCRPC. All patients had prostate
adenocarcinoma confirmed by pathology. Clinical data were collected from each medical record. Tumor grades were classified by Gleason grading system according to 2014 ISUP consensus [11]. Extent of disease on bone scan (EOD) [12] was used for objective semi-quantitative classifications of osseous metastases of bone scan: 0 = normal or abnormal due to benign bone disease; 1 = fewer than 6 bony metastases, each of which is less than 50% of the size of a vertebral body (1 lesion about the size of a vertebral body was counted as 2 lesions); 2 = from 6 to 20 bone metastases, sized as described above; 3 = more than 20 metastases but fewer than seen in a “superscan”; and 4 = “superscan” or its equivalent (i.e., more than 75% of the ribs, vertebrae, and pelvic bones). Surgical sites for MSCC were classified to five sites described below; “Cervical spine”, “Cervical-thoracic spine”, “Thoracic spine”, “Thoracic-lumbar spine”, and “Lumbar spine”.

Surgical procedures and postoperative radiation therapies for SCC

Standard surgical procedures were posterior decompression and stabilization. Patients without mechanical instability and with preservation of sagittal alignment of spine were treated by decompression alone although the surgical procedures were depend on each surgeon. Postoperative radiation was not used in the patients with mHNPC. In contrast, postoperative radiation was recommended for patients with mCRPC if the patients’ status were tolerable for radiation therapy.

Medical treatments for PC

Standard medical therapy for mHNPC was androgen ablation therapy. No patients received cytotoxic agent or new androgen receptor targeted therapy (abiraterone and/or enzalutamide) for mHNPC. After failed to CRPC, bisphosphonate or denosumab, new androgen receptor targeted therapy, radium-223, and cytotoxic agent (docetaxel with steroids and/or canazitaxel with steroids) were used if these agents were approved in Japan when physician decide the use. Treatment sequence for mCRPC were depend on physician’s direction.

Evaluation of functional outcome

Frankel grading classifications [13] were used for preoperative and postoperative functional evaluation. Frankel grading classifications revealed the extent of the neurological/functional deficit caused by spinal cord injury. It suggested by Frankel et al. in 1969 [13]. In briefly described as
following about Frankel grading classifications which segregated five categories: (A); no function, (B); sensory only, (C); some sensory and motor preservation, (D); useful motor function, and (E); normal. Frankel D and E indicated ambulatory.

Evaluation of oncological outcome

The Kaplan–Meier product-limit was used to estimate the overall survival (OS) distribution after surgery for MSCC. All analyses were conducted using IBM SPSS Statistics software for Windows, version 24 (IBM Corp., Armonk, NY, USA).

Ethics

The experimental procedures were conducted in accordance with the ethical standards of the Helsinki Declaration. This study was approved by the Institutional Review Board of Yokohama City University Medical Center and Yokohama City University Hospital.

Results

Patients’ characteristics

Table 1 showed patients’ characteristics. Median age of patients with mHNPC and mCRPC at the time of surgery for MSCC were 72 and 65, respectively. Median PSA at diagnosed as MSCC of patients with mHNPC and mCRPC were 910 ng/mL and 67 ng/mL, respectively. Sites of decompression surgery were cervical spine: 0 (0.0 %), cervical-thoracic spine; 0 (0.0 %), thoracic spine; 6 (75.0 %), thoracic-lumbar spine; 0 (0.0 %), and lumbar spine; 2 (25.0 %) in patients with mHNPC and cervical spine: 1 (9.1 %), cervical-thoracic spine; 2 (18.2 %), thoracic spine; 6 (54.5 %), thoracic-lumbar spine; 1 (9.1 %), and lumbar spine; 1 (9.1 %) in patients with mCPRC. Median time to decompression surgery from symptoms were 4 days in patients with mHNPC and 2 days in patients with mCRPC. Bone-targeted agents such as zoledronic acid and denosumab have been used in four (36.3 %) among men with mCRPC, while none of the patients with mHNCP received. Variables at initial diagnosis of prostate cancer were also listed in table 1.

Functional outcomes

Table 2 showed the functional outcomes evaluated by Frankel grade before and after decompression surgery among men with mHNPC. Although 2 out of 8 patients (25.0 %) with mHNPC were ambulatory
(Frankel grade D and E) preoperatively, 6 patients (75.0 %) were ambulatory postoperatively. Table 3 showed the functional outcome evaluated by Frankel grade before and after decompression surgery among men with mCRPC. Among 11 patients with mCRPC, only 3 patients (27.3 %) were ambulatory preoperatively, 6 patients (54.5 %) were ambulatory postoperatively.

Oncological outcomes

Fig. 1 revealed Kaplan-Meier curve for OS after decompression surgery among men with mHNPC and mCPRC. Median postoperative OS after decompression surgery among men with mHNPC and mCPRC were not reached and 8 months, respectively.

Discussions

MSCC from PC may cause of irreversible neurological impairment, gait disturbance, and worsen quality of life. So, MSCC is an oncologic emergency that require accurate diagnosis and rapid treatment [14]. When considering the treatment strategy for symptomatic MSCC, multidisciplinary approaches are needed [14]. As initial treatment for MSCC, glucocorticoid such as high dose dexamethasone is recommended for transient prevent the progress of neurological impairment from MSCC [15]. A few reports indicated that administration within 24–48 hours after appearance of neurological impairment could lead neurological recover [16, 17].

Definitive treatment for MSCC were surgery and radiation therapy. Patcchell et al. demonstrated that decompression surgery plus postoperative conventional external beam radiation was superior to treatment with radiation alone for MSCC from various cancer, by phase 3 randomized clinical trial [10].

Surgery for MSCC has been reported to result in rapid resolve of pain, neurological impairment, and maintain the quality of life of patients [14]. In determine the treatment strategy for MSCC, patients’ prognosis, general health status, neurologic/mechanical function, and surgical morbidity and mortality should be considered [9, 14, 18, 19]. Several tools for predicting survival among men treated with surgery for MSCC has been reported. Revised Tokuhashi score is commonly used for preoperative scoring system to predict survival and evaluate the indication of surgery [20]. This score is consist of 6 variables; General condition (performance status), Number of extraspinal bone metastases foci,
Number of metastases in vertebral body, Metastases to the major internal organs, Primary site of the cancer, and Palsy. Those scores were rating from 0 to 15 and if the patient’s score was 0–8, they reported that conservative treatment was recommended because 89 % of patients with score 0–8 have survival period less than 6 months. In contrast, 87.5 % of patients with score 12–15 have survival period of 1 year or more and surgery for MSCC is recommended. In general, palliative surgery such as decompression surgery are performed for MSCC, however, excisional surgery are considered in highly selected patients with favorable prognosis and good general health status such as patient with score 12–15 [20]. PC-specific prognostic nomogram for mHNPC [3] or mCRPC [21] also useful for predict survival and provide significant information for orthopedic surgeon when considering the indication of surgery and determine surgical procedure.

Preoperative neurological/mechanical function are also important factors when considering treatment strategy for MSCC. Clarke et al. reported that [9] only one patients with preoperative Frankel Class B patient had good functional outcome (Frankel Class D or E) after surgery, although majority of patients with preoperative Frankel Class C, D, or E showed favorable postoperative functional outcome. In our study, every 1 patient with Frankel A and B were performed surgery and they also showed unfavorable functional outcome postoperatively.

Although selection bias is not ruled out, preoperative Frankel A or B could be carefully considered the indication of surgery.

In present study, evsen though 2 out of 8 patients with mHNPC were ambulatory preoperatively, six out of 8 patients were ambulatory postoperatively and median survival after surgery for MSCC was not reached. Crnalic et al. also reported [22] that 13 patients treated with surgery for MSCC from mHNPC have long survival (median OS after surgery; not reached) and nine out of 12 patients were ambulatory postoperatively even though one out of 12 patients were ambulatory preoperatively.

Recovery of gait function may contribute to increasing quality of life especially in patients with good prognosis. Although there were few clinical evidences, surgery for MSCC among men with mHNPC were beneficial in appropriate selected patients for both favorable quality of life and good prognosis. While patient treated with MSCC from mCRPC have only 8 months of median survival after surgery in
present study. Crnalic et al. also reported [22] that 41 patient treated with surgery for MSCC from mCRPC only have 5 months of median survival. They also reported that even though five out of 41 patients were ambulatory preoperatively, 23 patients out of 41 patients were ambulatory postoperatively and unfortunately, 6 out of 41 patients were died with 4 weeks after surgery [22]. Survival benefit obtained from surgery for MSCC among patients with mCRPC might be low, however, these patients might be surgical candidate for good quality of life in highly selected situations [9, 22, 23].

Our current study was retrospective fashion, small cohort, and some other study limitations exist, we demonstrated that decompression and reconstruction surgery for symptomatic MSCC form PC might contribute favorable functional outcome among men with mHNPC and mCRPC. However, its role for improving the oncological outcome remains unclear. Anyway, treatment strategy should be made by shared-decision making among patients, urologists, radiation oncologists, and orthopedic surgeons.

Conclusions
Our retrospective study demonstrated that decompression and reconstruction surgery for symptomatic MSCC form PC might contribute favorable functional outcome among men with PC. Hormone naivety, mechanical/neurological function might be correlated with outcome after surgery. Treatment strategy should be made by shared-decision making among patients, urologists, radiation oncologists, and orthopedic surgeons.

List Of Abbreviations
Metastatic spinal cord compression (MSCC)
Prostate cancer (PC)
Metastatic hormone naïve prostate cancer (mHNPC)
Metastatic castration-resistant prostate cancer (mCRPC)
Prostate-specific antigen (PSA)
Extent of disease on bone scan (EOD)
Overall survival (OS)

Declarations
Ethics approval and consent to participate: IRB approval for Yokohama City University.
Consent for publication: We obtained IRB approval, including publication allowance.

**Availability of data and materials:** Due to ethical restrictions, the raw data underlying this paper are available upon request to the corresponding author.

**Competing interests:** The authors declare that they have no competing interests

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**Authors’ contributions:** Conceived and designed the study: TK, MY, HU, YM. Analyzed data: TK, YM. Wrote the paper: YM.

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**Tables**

Table 1. Patients' characteristics
| Variables at initial diagnosis of prostate cancer | Patients with mHNPC (n=8) | Patients with mCRPC (n=11) |
|-----------------------------------------------|---------------------------|---------------------------|
| Median prostate-specific antigen (range), ng/mL | 910 (98-8900)            | 232 (1)                  |
| Biopsy Gleason scores, n (%):                  |                           |                           |
| ≤7                                            | 0 (0.0 %)                 | 2 (1)                    |
| 8-10                                          | 5 (62.5 %)                | 9 (8)                    |
| Unknown                                       | 3 (37.5 %)                | 0 (0)                    |
| Extent of disease on bone scan:                |                           |                           |
| 0                                             | 0 (0.0 %)                 | 4 (3)                    |
| 1                                             | 2 (25.0 %)                | 2 (1)                    |
| 2                                             | 1 (12.5 %)                | 1 (1)                    |
| 3                                             | 1 (12.5 %)                | 1 (1)                    |
| 4                                             | 0 (0.0 %)                 | 0 (0)                    |
| Unknown                                       | 4 (50.0 %)                | 3 (2)                    |
| Variables at decompression surgery:            |                           |                           |
| Median age (range), years:                     | 72 (62-78)                | 65 (1)                   |
| Median prostate-specific antigen (range), ng/mL| 910 (98-8900)            | 67 (0)                   |
| Lesion of decompression surgery, n (%):        |                           |                           |
| Cervical spine                                | 0 (0.0 %)                 | 1 (1)                    |
| Cervical-thoracic spine                       | 0 (0.0 %)                 | 2 (1)                    |
| Thoracic spine                                | 6 (75.0 %)                | 6 (5)                    |
| Thoracic-lumbar spine                         | 0 (0.0 %)                 | 1 (1)                    |
| Lumbar spine                                  | 2 (25.0 %)                | 1 (1)                    |
| Median time to decompression surgery from symptoms occurrence (range), days | 4 (0-8) | 2 (1) |
| The use of bone-targeted agents*, n (%):       | 0 (0.0 %)                 | 4 (3)                    |

mHNPC; metastatic hormone-naïve prostate cancer, mCRPC; metastatic castration-resistant prostate cancer

*Zoledronic acid and denosumab

Table 2. Surgery for metastatic spinal cord compression from metastatic hormone-naïve prostate cancer; Functional outcome.
Table 3. Surgery for metastatic spinal cord compression from metastatic castration-resistant prostate cancer; Functional outcome.

| FRANKEL Grade | Preoperative | Postoperative | Number |
|---------------|--------------|---------------|--------|
|               | A            | B             | C      | D    | E    | Tc   |
| A             |              |               |        |      |      |      |
| B             |              |               |        |      |      |      |
| C             |              |               |        | 1    | 3    |      |
| D             |              |               |        |      | 2    |      |
| E             |              |               |        |      |      |      |

Figures
Figure 1

Kaplan-Meier curve for overall survival (OS) among men treated with decompression surgery for MSCC originating from metastatic hormone-naïve prostate cancer (mHNPC, n=8) and metastatic castration-resistant prostate cancer (mCRPC, n=11). Median postoperative OS after surgery was not reached in men with mHNPC and 8 months in men with mCRPC. Blue line indicated survival for men with mHNPC and green line indicated survival for men with mCRPC.