Is age an independent risk factor for perioperative mortality and morbidity after radical prostatectomy? Analysis of the American college of surgeons national surgical quality improvement program database

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ABSTRACT

Objectives: To assess the safety and surgical outcomes of radical prostatectomy (RP) when looking at age as an independent risk factor of perioperative mortality and morbidity. Patients and methods: A retrospective cohort study was performed using American College of Surgeons National Surgical Quality Improvement Program database. Patients who underwent a RP from 2008 to 2015 were identified. They were divided into three groups based on their age 15 group at the time of surgery. Patients’ characteristics were compared across the three following age groups: 74 years. The correlation between the three different age groups and their respective 30-day postoperative mortality and morbidity were assessed using logistic regression. Unadjusted and adjusted odds ratios (ORs) were estimated. Results: A total of 43025 patients were identified, 81.7% were aged 74 years. Overall, 102 patients died in the 30-day postoperative period. Univariate and multivariate analysis showed a significant increase in the 30-day postoperative mortality from 0.1% to 0.4% to 1.3% in the three different age groups 74 years, respectively. In addition, there was a significant increase in postoperative complications in the group of patients aged >74 years. A higher risk of complications 25 related to cardiac (OR 2.18 in age group 70–74 vs OR 7.45 in age group >74 years), respiratory (OR 2.36 vs OR 5.91), neurological (OR 2.28 vs OR 3.44), wound infections (OR 1.49 vs OR 3.25), and sepsis (OR 1.54 vs OR 2.64) were seen with the youngest group taken as a reference. Conclusion: Age is an independent risk factor for perioperative mortality and morbidity after RP in elderly patients. Therefore, age should be considered in the decision making of therapeutic options for patients with prostate cancer.

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Introduction

Prostate cancer (PCa) is the most commonly diagnosed male cancer; it is one of the leading causes of cancer mortality worldwide [1,2]. Due to the increase in men’s life-expectancy, diagnosing PCAs at an older age has increased significantly and is expected to continue to increase. There are several therapeutic regimens available for elderly men diagnosed with PCAs ranging from active surveillance (AS) or watchful waiting, focal therapy, radiation therapy, and surgery. A surgical approach, radical prostatectomy (RP), entails the possibility of perioperative morbidity and mortality, especially in the elderly population.

Most studies exploring treatment regimens for PCa have focussed on men aged <75 years. However, in men with a life-expectancy >10 years, Richstone et al. [3] demonstrates the importance of careful patient selection for RP. Carefully selected men that are aged >70 years undergoing RP or radiotherapy have similar oncological outcomes and quality adjusted life-expectancy when compared to younger men. As such, patient selection as well as treatment modality selection is still uncertain and multifactorial [3].

There is a general tendency in PCa to undertreat the disease owing to the fact that it is generally an indolent disease; however, the International Society of Geriatric Oncology (SIOG) recommends that older patients with PCa should be managed according to their general health status and comorbidities rather than age alone [4–8]. Furthermore, an increased age of diagnosis is associated with more aggressive disease characteristics [9]. RP remains the ‘gold standard’ for the treatment of localised PCa, yet perioperative complications remain a major concern in regards to the surgical option in treating PCa, especially in elderly patients.
In our present analysis of the American College of Surgeons (ACS) National Surgical Quality Improvement Program database (NSQIP), we compared postoperative mortality and morbidity in patients undergoing RP for PCa in different age groups in order to determine whether age is an independent risk factor of perioperative mortality and morbidity.

Patients and methods

Our retrospective cohort used data from the ACS NSQIP database (Figure 1). The database is a validated registry of outcomes on 30-day postoperative surgical mortality and morbidity from participating hospitals around the USA [10,11]. It includes data on demographics, perioperative variables, and 30-day postoperative outcomes for adult patients undergoing major surgery. A team of trained surgical clinical reviewers collected patient data. In addition, a comprehensive training for data review, regular conference calls, and annual meetings ensure proper quality of the data [12].

Patients who underwent a RP (open, laparoscopic, robot-assisted) from 2008 to 2015 were identified from the ACS NSQIP. Patients’ were divided into three groups based on their age at the time of RP. Patients’ characteristics were compared across the three following age groups: <70, 70–74, and >74 years. The correlation between the three different age groups and their respective 30-day postoperative mortality and morbidity was assessed using logistic regression. Frequency and percentage were used to describe categorical variables, whereas mean and standard deviation (SD) were used for continuous ones. Categorical variables were compared across the aforementioned age groups using the chi-squared test. ANOVA was used for the continuous ones. The lowest age category was set as a reference; separate logistic regression models were used for each outcome, upon which unadjusted and adjusted odds ratios (ORs) were estimated using the youngest age group as the reference group. Clinically potential confounders were considered for the multivariate analysis of each of the outcomes. All analyses were performed using Statistical Analysis System (SAS) (SAS Institute Inc., Cary, NC, USA). P values were two-sided and statistical significance was set at P < 0.05.

Results

Over a span of 7 years, from 2008 to 2015, 43,025 patients underwent a RP in the USA. This included open, laparoscopic and robot-assisted surgery. In all, 81.7% of patients were aged <70 years, 12.6% were aged 70–74 years, and 5.5% were aged >74 years. Comorbidities amongst patients at 30-days preoperatively were evaluated. They ranged from no comorbidities to hypertension (51.6%), obesity (body mass index [BMI] >30 kg/m², 35.4%), diabetes (12.7%), chronic obstructive pulmonary disease (2.5%), and congestive heart failure (0.1%) (Table 1).

Mortality

Overall, the 30-day postoperative mortality rate was 0.2% across the three different age groups. The univariate analysis showed a significant increase in the crude 30-day mortality amongst the groups. It was 0.1% in the <70 years age group, 0.4% for those aged 70–74 years, and 1.3% for those aged >74 years (Table 2; Figure 1).

The multivariate analysis accounted for patient comorbidities such as hypertension, BMI, diabetes, chronic obstructive pulmonary disease, and congestive heart failure. Similarly, the 30-day postoperative mortality risk after RP was associated with older age. In comparison to the <70 years age group, the 70–74 years age group was associated with a 3.05-fold mortality rate increase, whereas the >74 years age group was associated with an 8.52-fold mortality rate increase (Table 3).

Morbidity

Overall, 2,113 patients had at least one perioperative complication. In all, 4% of the <70 years age group had

Figure 1. Risk of complications between different age groups.
Table 1. Demographics.

| Variable | All (N = 43,025) | Age group, years | P |
|----------|-----------------|-----------------|---|
| n/N (%)  |                 | <70 (n = 35,187) | 70–74 (n = 5451) | >74 (n = 2387) |
| Race     |                 |                 |                 |               |
| White    | 31,747/37,036 (85.7) | 25,733/30,416 (84.6) | 4095/4551 (90.0) | 1919/2069 (92.8) | <0.001 |
| African-American | 4229/37,036 (11.4) | 3854/30,416 (12.7) | 293/4551 (6.4) | 82/2069 (4.0) |               |
| Others   | 1060/37,036 (2.9) | 829/30,416 (2.7) | 163/4551 (3.6) | 68/2069 (3.3) |               |
| ASA classification | | 1432/35,125 (4.1) | 121/4551 (2.2) | 24/2383 (1.0) | <0.001 |
| I       | 1577/42,953 (3.7) | 1470/35,125 (4.1) | 122/4551 (2.7) | 24/2383 (1.0) | <0.001 |
| II      | 25,012/42,953 (58.2) | 21,470/35,125 (61.1) | 2709/4551 (48.9) | 833/2383 (35.0) |               |
| III     | 15,832/42,953 (36.9) | 11,891/35,125 (33.9) | 526/4551 (46.4) | 1415/2383 (59.4) |               |
| IV      | 332/42,953 (1.2) | 332/35,125 (1.0) | 89/4551 (1.6) | 111/2383 (4.7) |               |
| Transfusion >4 units PRBCs in 72 h before surgery | 99/43,025 (0.2) | 47/35,187 (0.2) | 16/5451 (0.3) | 36/2387 (1.5) | <0.001 |
| Hypertension requiring medication | 42,750/42,905 (99.6) | 34,986/35,086 (99.7) | 5409/5434 (99.5) | 2355/2385 (98.7) | <0.001 |
| Partially dependent | 135/42,905 (0.3) | 86/35,086 (0.2) | 3/5434 (0.1) | 1/2385 (0.1) |               |
| Totally dependent | 20/42,905 (0.0) | 14/35,086 (0.0) | 0/5434 (0.0) | 0/2385 (0.0) |               |
| BMI >30 kg/m² | 5857/43,025 (13.6) | 5203/35,187 (14.8) | 485/5451 (8.9) | 169/2387 (7.1) | <0.001 |
| Diabetes mellitus with oral agents or insulin | 5445/43,025 (12.7) | 4146/35,187 (11.8) | 881/5451 (16.2) | 418/2387 (17.5) | <0.001 |
| Systemic sepsis | 121/43,025 (0.3) | 83/35,187 (0.2) | 16/5451 (0.3) | 22/2387 (0.9) |               |

CHF, Congestive heart failure; COPD, chronic obstructive pulmonary disease; PRBCs, packed red blood cells.

Discussion

Most (64%) of the newly diagnosed PCA cases in the USA were diagnosed in men aged >65 years, while 23% of cases were diagnosed in men >75 years. With the continuous improvement in overall life expectancy, a 70-year-old man’s average life-expectancy is now reaching 13 years [13]. As such, management of PCA should be tailored in a way that ensures optimal management of disease whilst delaying mortality and minimising treatment-related morbidities.

In the USA, 16% of men diagnosed with PCs die despite available treatments, while PCa is a direct cause of 3% of all male mortality [14]. Furthermore, the disease has an indolent course with a median time of 8 years from biochemical failure to metastasis and 5 years from metastasis to death [15]. For many years now, RP has been the modality of choice for localised PCs in surgically fit men. The aim of surgery is achieving the trifecta of survival, continence preservation, and erectile function preservation [16].
Table 2. Univariate analysis.

| Variable                        | All                 | Age group, years | Unadjusted OR (95% CI) |
|---------------------------------|---------------------|------------------|------------------------|
|                                 | (N = 43,025)        | (<70)            | (70–74)                | (>74)                  |
| Mortality                       | 106 (2.0)           | 59 (0.1)         | 24 (0.4)               | 32 (1.3)               |
| Composite morbiditya            | 2113 (4.9)          | 1420 (4.0)       | 324 (5.9)              | 369 (15.3)             |
| Wound                           | 720 (1.7)           | 495 (1.4)        | 116 (2.1)              | 109 (4.6)              |
| Cardiac                         | 180 (0.4)           | 94 (0.3)         | 34 (0.6)               | 52 (2.2)               |
| Respiratory                     | 387 (0.9)           | 213 (0.6)        | 78 (1.4)               | 96 (4.0)               |
| Urinary                         | 289 (0.7)           | 185 (0.3)        | 55 (1.0)               | 49 (2.0)               |
| CNSb                            | 73 (0.3)            | 46 (0.2)         | 16 (0.5)               | 11 (0.8)               |
| Thromboembolism                 | 613 (1.4)           | 444 (1.3)        | 78 (1.4)               | 91 (3.8)               |
| Sepsis                          | 719 (1.7)           | 459 (1.3)        | 113 (2.1)              | 147 (6.2)              |
| Bleeding                        | 2875 (6.7)          | 1860 (5.3)       | 482 (8.2)              | 566 (23.7)             |
| Return to operating room        | 701 (1.6)           | 506 (1.4)        | 101 (1.8)              | 94 (3.9)               |

| Variable                        | All                 | Age group, years | Unadjusted OR (95% CI) |
|                                 | (n = 54,51)         | (n = 23,87)      |                        |
| Mortality                       | <0.001              | 3.11 (1.91–5.06) |                        |
| Composite morbiditya            | <0.001              | 1.51 (1.24–1.87) |                        |
| Wound                           | <0.001              | 1.52 (1.24–1.87) |                        |
| Cardiac                         | <0.001              | 2.34 (1.38–3.47) |                        |
| Respiratory                     | <0.001              | 2.38 (1.84–3.09) |                        |
| Urinary                         | <0.001              | 1.93 (1.42–2.61) |                        |
| CNSb                            | <0.001              | 2.35 (1.33–4.16) |                        |
| Thromboembolism                 | <0.001              | 1.14 (0.89–1.45) |                        |
| Sepsis                          | <0.001              | 1.60 (1.30–1.97) |                        |
| Bleeding                        | <0.001              | 1.61 (1.44–1.79) |                        |
| Return to operating room        | <0.001              | 1.29 (1.04–1.60) |                        |

*Composite morbidity considered positive if any of wound, cardiac, respiratory, urinary, CNS, sepsis or thromboembolism is positive.

bSample size: 25,228.
PCAs. As shown in the two aforementioned studies, surgery did not significantly alter survival outcomes compared to observation [20,21]. As such, AS decreases the risk of overtreatment through careful patient selection. Criteria for AS include patients with low-risk disease (low-volume Gleason 6 and not more than T2 disease clinically), high level of compliance, and a tolerable anxiety regarding the disease taking into account patient comorbidities and life expectancy [22,23]. It is imperative to mention that AS is discouraged for intermediate- and high-risk PCAs.

The limitations of our present study are mostly related to our data. The data are crude and the possibility of subgroup analysis was limited. Cause–effect relationships pertaining to patient characteristics or disease pathology (Gleason grade, PSA levels, stage) were not assessed except those related to age. In addition, subgroup analysis comparing the impact of surgical technique in RP was not done (i.e. open approach vs laparoscopic or robot-assisted). Another caveat of our present study was the inability to assess postoperative continence or potency.

Conclusion

Our present study sheds light on the effect of age as an independent factor in determining risk of perioperative mortality and morbidity following RP. In conclusion, age by itself should play a significant role in selecting surgical candidates with PCa, whereby older individuals are at higher risk for morbidity and even mortality; hence alternative therapies could be considered.

Authors’ contributions

Merhe Ali and Nasr Rami conceived the project. Hout Mohammad, Abou Heidar Nassib and Jose M. El-Asmar performed the pertinent literature review and wrote a significant part of the manuscript. Mailhac Aurelie and Tamim Hani and Jaafar Rola performed the statistical analysis and devised the methodology. Merhe Ali, Hout Mohammad, Abou Heidar Nassib, Jose M. El-Asmar, and Nasr Rami finished writing the manuscript.

All authors agreed on the final manuscript before submission.

Disclosure statement

The authors listed certify that they have no affiliation with and are not involved with any organization or entity with any financial interest or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethics statement

Our Institution is a participating site in the ACS NSQIP database. No Institutional Review Board acceptance was required for the project.

Data are available upon request.

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