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Causes of Prostate Cancer Recurrence After Radical Prostatectomy

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Abstract:
Prostate cancer recurrence following radical prostatectomy (RP) poses significant challenges for patient management and long-term outcomes. The objective of this study was to summarize the main factors associated with prostate cancer recurrence after radical prostatectomy. A scoping review was conducted using the PubMed database with keywords including 'prostate cancer recurrence after radical prostatectomy,' 'biochemical recurrence,' and 'surgical margins.' The search was limited to English-language studies published between 2020–2025. Inclusion criteria focused on clinical and case report studies involving recurrence post-RP with a minimum of 12-month follow-up. A total of 4,736 articles were identified, with 23 studies meeting all eligibility criteria. Recurrence was primarily associated with positive surgical margins, Gleason score, PSA kinetics, and molecular markers such as gene signatures and inflammation-related profiles. Salvage radiotherapy, especially when administered early, showed improved outcomes. Genetic and imaging advances contributed to improved risk stratification. The recurrence of prostate cancer after RP is influenced by surgical, biological, and individual patient factors. Early detection and risk-adapted interventions are crucial in improving survival and minimizing progression.

Keywords: Prostate cancer; Radical prostatectomy Biochemical recurrence; Surgical margin; Salvage therapy

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INTRODUCTION

Prostate cancer is a significant health concern for men worldwide and often requires interventions such as radical prostatectomy (RP) for localized forms (Chan et al., 2021). However, rates of recurrence following such treatments present a considerable challenge. Recurrences can manifest as either biochemical recurrence (BCR) or clinical recurrence, leading to anxiety among patients and necessitating a comprehensive understanding of the underlying causes and predictive factors for recurrence post-surgery (He et al., 2022; Wei et al., 2022). Utilizing data from various studies, this discourse will elucidate the multifaceted reasons behind prostate cancer recurrence after radical prostatectomy, highlighting the interaction between biological markers, surgical techniques, and patient demographics.

Biochemical recurrence (BCR) signifies a concerning clinical outcome where prostate-specific antigen (PSA) levels rise post-surgery, often indicating the resurgence of cancer cells. Statistical analyses show that BCR rates can range from approximately 15% to 30% following radical prostatectomy, with certain patient groups experiencing even higher rates due to aggressive cancer characteristics (Wei et al., 2022; Kutluhan et al., 2021; Sato et al., 2020). Understanding individual patient risk profiles is essential, where factors such as age, PSA levels prior to surgery, and Gleason scores play critical roles in determining the likelihood of recurrence. For instance, investigators have indicated that patients with higher pre-operative PSA levels and higher Gleason scores are particularly at risk (Kutluhan et al., 2021; Sato et al., 2020).

The biological architecture of prostate cancer presents additional complexities. MicroRNAs (miRNAs), especially miR-148a-3p and miR-485-5p, have been implicated in cancer progression and recurrence, suggesting a potential pathway through which these molecules may serve as biomarkers for recurrence (He et al., 2022; He et al., 2022). Genetic factors also unveil varying incidences of prostate cancer among different ethnicities; notably, African American men exhibit higher incidence rates compared to their Caucasian counterparts, indicating a potential genetic predisposition (Sung et al., 2021; Nyame et al., 2016).

Furthermore, the impact of surgical technique on recurrence cannot be overlooked. Robot-assisted radical prostatectomy (RARP) has gained traction due to its advantages, including reduced intraoperative complications and blood loss (Nathan et al., 2021; Nossiter et al., 2018). Despite these procedural advancements, the achievement of negative surgical margins—a critical factor in minimizing the likelihood of recurrence—remains a focal point of surgical practice. Data suggests that RARP may be associated with a lower rate of positive surgical margins compared to traditional open approaches, thereby potentially diminishing the risk of recurrence in appropriately selected patients (Nathan et al., 2021; Nossiter et al., 2018).

The presence of surgical complications, such as those arising from previous therapies for other conditions (e.g., adhesions from rectal surgery), can contribute to postoperative recurrence (Imasato et al., 2024). These complications may complicate the surgical field and hinder the surgeon's ability to achieve clean margins, thus increasing recurrence rates. Therefore, managing patient histories regarding previous treatments and anticipating potential complications is crucial in surgical planning and execution. In addition to surgical considerations, patient lifestyle and postoperative recovery have significant implications for recurrence. Physical activity has been linked to improved outcomes following radical prostatectomy (Kazan et al., 2023; Sung et al., 2021). Evidence suggests that engaging in regular physical activity may enhance recovery, with positive correlations found between physical fitness and lower rates of recurrence. This underscores the need for comprehensive postoperative care that extends beyond the surgical intervention itself.

Continued research and large cohort studies are critical for establishing definitive predictive models that consider a spectrum of factors, from biological to lifestyle attributes (Kutluhan et al., 2021). Such models could advance the understanding of recurrence and inform clinical decision-making, ultimately leading to better patient outcomes. The recurrence of prostate cancer after radical prostatectomy is a complex issue influenced by a multitude of factors, including biological, surgical, and lifestyle elements. This intricate interplay necessitates ongoing research to refine treatment techniques and postoperative care strategies, aiming to improve survival and quality of life for men facing this malignancy. This study aimed to review the causes of prostate cancer recurrence after radical prostatectomy. The objective of this study was to summarize the main factors associated with prostate cancer recurrence after radical prostatectomy.

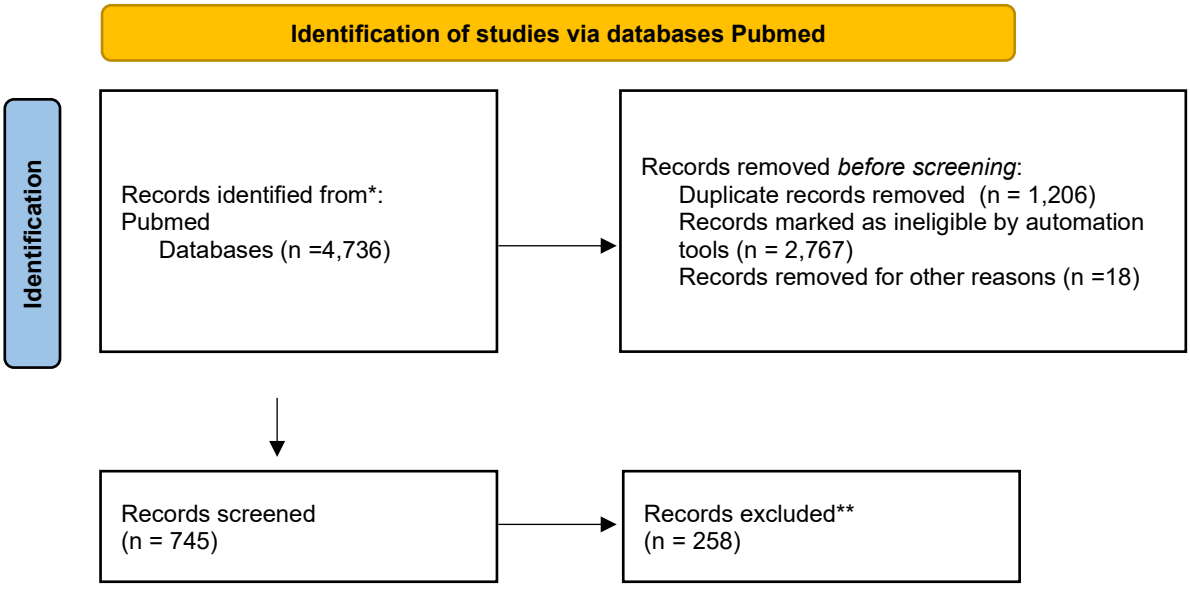
METHOD

This paper reviewed clinical studies and case reports to obtain more representative results. The review was conducted by searching the PubMed database using keywords, including 'prostate cancer recurrence after radical prostatectomy,' 'biochemical recurrence prostate cancer,' 'surgical margin prostate cancer case reports,' and 'predictive factors for prostate cancer recurrence.' The search was refined by limiting the publication years to the last 5 years (2020–2025) to ensure more up-to-date and relevant findings. The review aimed to answer the question of what biological, clinical, or surgical factors contribute to prostate cancer recurrence following radical prostatectomy.

The keyword 'prostate cancer recurrence after radical prostatectomy' resulted in 1,318 documents. The keyword 'biochemical recurrence prostate cancer' resulted in 2,948 documents. The keyword 'surgical margin prostate cancer case reports' resulted in 13 documents. The keyword 'predictive factors for prostate cancer recurrence' resulted in 484 documents. In total, 4,736 documents were identified through the PubMed database search.

The inclusion criteria for this scoping review were studies and case reports published between 2020 and 2025, written in English, and reporting recurrence of prostate cancer following radical prostatectomy. Articles were included if they provided clinical data on recurrence in terms of biochemical recurrence, surgical margin status, or pathological predictors. The population criteria included male patients who had undergone radical prostatectomy for localized prostate cancer. The outcome criteria included recurrence defined by rising PSA levels or clinical evidence of cancer return, with follow-up data extending at least 12 months postoperatively.

All 4,736 documents were screened by title to eliminate duplicates and irrelevant studies. Based on title review, 745 items were considered relevant. These 745 were then screened by abstract, and 258 were excluded for lacking direct focus on recurrence or not meeting the population criteria. The remaining 157 items were sought for full-text retrieval, and all were successfully retrieved. Upon full-text review, 134 of these did not meet the inclusion criteria—either due to inadequate follow-up (reason 1), absence of recurrence outcomes (reason 2), or non-prostatectomy populations (reason 3). As a result, 23 studies were deemed eligible for inclusion in this review. Figure 1 shows the PRISMA Sc-R diagram.



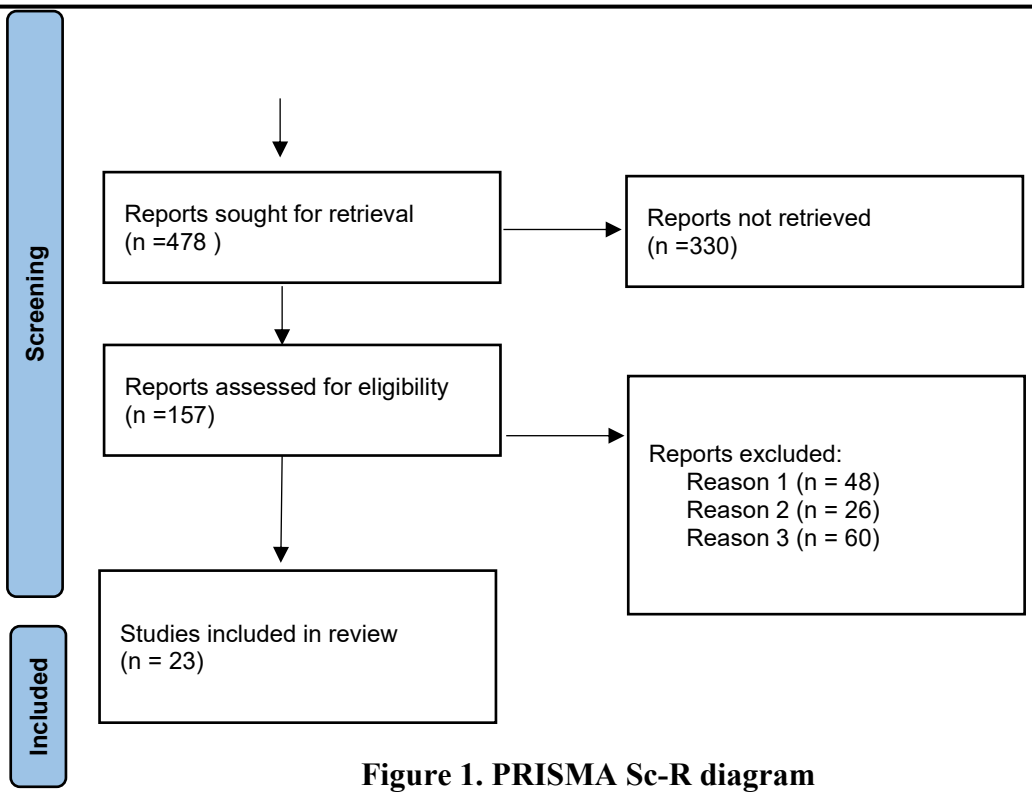


Figure 1. PRISMA Sc-R diagram

RESULT AND DISCUSSION

In prostate cancer treatment, maximizing therapeutic efficacy while minimizing recurrence risk is paramount, particularly post-radical prostatectomy (RP). This analysis utilizes the PICO framework to evaluate key factors influencing biochemical recurrence (BCR) after RP. The presence of positive surgical margins (PSM) significantly correlates with increased BCR risk, influenced by factors such as pathological stage, Gleason score, and the surgical approach employed (Yang et al., 2021; , Guo et al., 2024). Moreover, systemic inflammatory markers and genetic signatures have been proposed as potential predictive biomarkers for BCR, thereby guiding postoperative management (Miyazaki et al., 2022; , Aldakheel et al., 2025). A detailed understanding of patient characteristics, including age, comorbidities, and previous treatment history, aids in tailoring surveillance and intervention strategies for enhanced outcomes post-surgery (Kryvenko et al., 2021; , Siech et al., 2024). Therefore, an efficient risk stratification approach based on these variables could significantly improve patient prognostication and therapeutic decision-making (Cai et al., 2022; , Roberts et al., 2022). Table 1 shows the PICO framework analysis related to prostate cancer recurrence after radical prostatectomy.

Table 1. PICO framework analysis

Reference	Population	Intervention	Comparison	Outcome
Yingxin Cai, Jingwei Lin, Zuomin Wang et al. 2022 Front. Oncol.	Prostate cancer patients from The Cancer Genome Atlas (TCGA) and the MSKCC database although the specific number of patients is not directly provided.	involves monitoring high-risk prostate cancer patients more closely and administering early salvage radiotherapy or combined androgen deprivation therapy (ADT) to prevent biochemical recurrence.	Provides a comparative analysis of traditional clinicopathological parameters versus a newly developed lipid metabolism-related gene signature in predicting biochemical recurrence in prostate cancer patients after radical prostatectomy indicating that the latter may offer enhanced prognostic accuracy.	The development and validation of a 6-gene lipid metabolism-related gene signature that effectively predicts biochemical recurrence in prostate cancer patients after radical prostatectomy thereby enhancing risk stratification and potential treatment personalization
Ugo Giovanni Falagario, Ahmad Abbadi, Sebastiaan Remmers et al. 2023JAMA Netw	16311 male patients with 10364 undergoing radical prostatectomy and 5947 undergoing radiotherapy	Evaluation of biochemical recurrence (BCR) following either radical prostatectomy or radiotherapy in male patients with prostate cancer	Focuses on the 15-year cumulative incidences of biochemical recurrence after radical prostatectomy versus radiotherapy demonstrating differing risk profiles for prostate cancer-specific mortality based on EAU-BCR stratification.	Indicates that while low-risk biochemical recurrence (BCR) after radical prostatectomy is associated with very low prostate cancer-specific mortality low-risk BCR after radiotherapy carries a significant risk of mortality suggesting the need for improved risk stratification and tailored treatment approaches.
Carolin Siech, Mike Wenzel, Carsten Lange et al. 2024 Medicina	821 patients with prostate cancer who underwent radical prostatectomy between January 2014 and June 2023	Radical prostatectomy (RP) as a treatment for patients with prostate cancer classified under a well-established guideline-recommended curative approach.	While prostate volume significantly predicts biochemical recurrence (BCR) after radical prostatectomy age and body mass index (BMI) do not show significant associations with BCR.	Higher prostate volume independently predicts biochemical recurrence (BCR) after radical prostatectomy while age and body mass index (BMI) were not significantly associated with BCR.

Yu Miyazaki, Takayuki Goto, Xin Li et al. 2022 Cancer Medicine	11 patients with prostate cancer specifically analyzed for SLPI expression in hormone naive and castration-resistant conditions	Analysis of secretory leukocyte protease inhibitor (SLPI) expression as a potential biomarker for predicting prostate cancer recurrence and progression particularly in castration-resistant prostate cancer (CRPC) models.	SLPI expression is significantly higher in castration-resistant prostate cancer (CRPC) cell lines compared to parental lines and its elevated levels correlate with worse prognosis in localized prostate cancer highlighting its potential as a biomarker for cancer progression.	Secretory leukocyte protease inhibitor (SLPI) expression serves as an independent risk factor for prostate-specific antigen recurrence and might predict disease progression in prostate cancer patients after surgery and hormonal therapy.
Adalgisa Guerra, Filipe Caseiro-Alves, Kris Maes et al. 2023 Cancers	177 participants who underwent robotic-assisted radical prostatectomy (RARP) and had a follow-up exceeding 6 months post-surgery.	The intervention is N/A as the study primarily utilized retrospective data analysis for predictive modeling rather than implementing a direct intervention.	Evaluates the differences in biochemical recurrence-free survival among patients with adverse MRI features versus those without specifically within low/intermediate-risk groups.	Adverse MRI features such as macroscopic extracapsular extension and high tumor capsular contact length are significant independent risk factors for biochemical recurrence after radical prostatectomy in prostate cancer patients.
Ching-Wei Yang, Hsiao-Hsien Wang, Mohamed Fayez Hassouna et al. 2021 Sci Rep	419 patients who underwent robot-assisted radical prostatectomy.	Robot-assisted radical prostatectomy (RARP) to investigate predictors of positive surgical margins and biochemical recurrence.	Positive surgical margin (PSM) outcomes associated with robot-assisted radical prostatectomy (RARP) against other surgical techniques identifying higher PSM likelihood at the bladder neck with RARP compared to open radical prostatectomy (ORP) and laparoscopic radical prostatectomy (LARP).	Preoperative prostate-specific antigen levels intraoperative blood loss and postoperative tumor stage are significant predictors of positive surgical margins and biochemical recurrence after robot-assisted radical prostatectomy in an Asian population.

Zhanpeng Liang, Sihong Lin, Huiqin Lai et al. 2023 Front. Oncol.	2731 male patients with 1374 receiving salvage radiotherapy combined with endocrine therapy and 1357 in the control group.	Combination of salvage radiotherapy (SRT) with endocrine therapy for patients experiencing biochemical recurrence after radical prostatectomy	Evaluates the efficacy and safety of salvage radiotherapy combined with endocrine therapy against salvage radiotherapy alone in patients with biochemical recurrence after radical prostatectomy.	Combination of salvage radiotherapy and endocrine therapy significantly improves biochemical progression-free survival and metastasis-free survival for patients with biochemical recurrence after radical prostatectomy while showing an increased risk of late adverse events.
Satoru Meguro, Nobuhiro Haga, Hitomi Imai et al. 2021 JSLS	324 consecutive patients with localized prostate cancer who underwent robot-assisted radical prostatectomy.	Limiting surgical duration during robot-assisted radical prostatectomy to reduce surgical stress and potentially lower biochemical recurrence rates in patients with positive surgical margins.	Association between prolonged surgical duration and biochemical recurrence in patients with positive surgical margins after robotic radical prostatectomy specifically contrasting patients who experienced recurrence with those who did not.	Prolonged surgical duration is significantly associated with biochemical recurrence in patients with positive surgical margins after robot-assisted radical prostatectomy
Paola Mapelli, Samuele Ghezzo, Cristiano Pini et al. 2023 Cancers	Consists of a selected cohort of biochemical recurrence prostate cancer patients after radical prostatectomy though the specific number of participants is not mentioned in the text provided.	Use of prostate-specific membrane antigen (PSMA)-targeted PET imaging for detecting biochemical recurrence in prostate cancer patients after radical prostatectomy.	The comparison in the article is N/A as it primarily discusses the predictors of PSMA PET positivity without directly comparing it to other imaging techniques.	PSMA-targeted PET imaging serves as the most accurate method for detecting and localizing disease relapses in prostate cancer patients with biochemical recurrence after radical prostatectomy.
Tanguy Perennec, L. Vaugier, Alain Tolédano et al. 2021 Cancers	48 patients who underwent salvage re-irradiation for local recurrence of prostate cancer after radical prostatectomy and radiation therapy.	Salvage re-irradiation with stereotactic radiation therapy for patients with local recurrence of prostate cancer after radical prostatectomy and external beam radiation therapy.	Limited due to confounding factors such as androgen deprivation therapy and a small patient sample size which hinder the assessment of imaging modality effectiveness.	While salvage re-irradiation for recurrent prostate cancer is associated with a significant biochemical response (83% positive at three months) it also involves considerable toxicity with 43% experiencing biochemical relapse by the end of follow-up.

Matthew J. Roberts, Mark D. Chatfield, George Hruby et al. 2022 BJU International	137 patients.	Involves the deployment of salvage radiotherapy (SRT) for men with biochemical recurrence of prostate cancer after radical prostatectomy combined with prostate-specific membrane antigen positron emission tomography (PSMA-PET) findings.	Contrasts regional nodal/distant metastasis on PSMA PET with local recurrence indicating a significantly higher hazard ratio for worse event-free survival (EFS) in patients with metastasis (HR 2.2; P = 0.002).	PSMA-PET findings and the use of salvage radiotherapy significantly predicted event-free survival in patients with biochemical recurrence after radical prostatectomy highlighting the potential for improving EAU risk grouping with PSMA-PET data.
Chun Li, Jie Zhu, Hexi Du et al. 2022 Front. Oncol.	The Cancer Genome Atlas (TCGA) cohort with specific differential expression analysis conducted on 25 pyroptosis-related genes but the exact sample size is not specified in the provided text	Identification and analysis of pyroptosis-related gene signatures for predicting prostate cancer recurrence with no specific clinical intervention mentioned; therefore it is N/A.	Evaluation of differentially expressed pyroptosis-related genes between prostate cancer tissues and normal tissues emphasizing how these gene signatures correlate with disease recurrence and survival outcomes in prostate cancer patients.	Expression signatures of pyroptosis-related genes can effectively predict prostate cancer recurrence offering potential as a novel prognostic tool for improving patient management.
Mats Ahlberg, Hans Garmo, Hans-Olov Adami et al. 2022BMJ Open	302 patients who underwent radical prostatectomy with a median age of 65 years and a median preoperative PSA level of 9.8 ng/mL.	Prospective analysis of follow-up protocols after radical prostatectomy aiming to determine if surveillance could be shortened for patients without biochemical recurrence.	Differing probabilities of biochemical recurrence metastases and prostate cancer death between patients with a Gleason score of ≤3+4 and ≥4+3 at 5 years post-radical prostatectomy.	Patients with favorable histopathology who remain free from biochemical recurrence five years after radical prostatectomy have a significant probability of avoiding future metastases and prostate cancer death suggesting that some can safely shorten follow-up monitoring.

Tanan Bejrananda, Pitchaya Pliensiri 2023 BMC Urol	370 localized and regional prostate cancer patients who underwent laparoscopic radical prostatectomy at Songklanagarind Hospital from January 2010 to December 2019	Development and validation of a predictive nomogram for biochemical recurrence-free survival (BCRFS) after laparoscopic radical prostatectomy (LRP) for localized and regional prostate cancer patients.	Development and validation of a predictive nomogram for biochemical recurrence-free survival (BCRFS) after laparoscopic radical prostatectomy contrasting patient outcomes based on various clinical factors.	Specific unfavorable factors significantly predict biochemical recurrence-free survival in prostate cancer patients post-laparoscopic radical prostatectomy contributing to a novel predictive nomogram with a concordance index of 0.78 for clinical decision-making.
H. Y. Guo, Lei Zhang, Yuan Shao et al. 2024PLoS ONE	Prostate cancer patients with a total of 3234 individuals analyzed.	Patients with positive surgical margin factors and specific pathological stages of prostate cancer should receive adjunct treatment and undergo more frequent monitoring.	Highlights how different parameters such as PGG at the PSM and pathological stage affect the risk of biochemical recurrence (BCR) post-radical prostatectomy emphasizing the need for tailored treatment strategies based on these variables.	Certain surgical margin parameters and pathological stages significantly increase the risk of biochemical recurrence in prostate cancer patients suggesting a need for tailored treatment and monitoring strategies for affected individuals.
Jia Jiang, Lei Chen, Xiaowei Ji et al. 2023 Research in Diagnostic and Interventional Imaging	100 patients with biochemical recurrence after radical prostatectomy	Use of (18F)-PSMA-1007 PET/CT for diagnosing biochemical recurrence after radical prostatectomy	Evaluates the diagnostic performance of (18F)-PSMA-1007 PET/CT against standard imaging methods in patients with biochemical recurrence after radical prostatectomy.	(18F)-PSMA-1007 PET/CT significantly improves diagnostic performance and influences treatment management in patients with biochemical recurrence after radical prostatectomy.
Chao Luo, Songzhe He, Haibo Zhang et al. 2022 Front. Genet.	1000 clinical samples from the TCGA cohort specifically focusing on patients with prostate cancer undergoing radical prostatectomy	Development of a prognostic classifier based on DNA methylation-driven differentially expressed genes to predict biochemical recurrence in prostate cancer patients after surgery.	Highlights the prognostic accuracy of a newly developed nomogram based on differential methylation-driven genes (DMGs) for predicting biochemical recurrence (BCR) in prostate cancer patients contrasting it with conventional factors like Gleason score and lymph node positivity.	Identification and validation of a nomogram for predicting biochemical recurrence-free survival in prostate cancer patients integrating seven key differentially expressed genes as independent prognostic factors.

Oleksandr N. Kryvenko, Oleksii A. Iakymenko, Luiz Paulo Guido et al. 2021 archives of pathology & laboratory medicine	171 cases of prostatic ductal adenocarcinoma after excluding 24 cases resulting in a final cohort of 147 cases for analysis.	Comparative analysis of radical prostatectomy outcomes between localized prostatic ductal adenocarcinoma and prostatic acinar adenocarcinoma matched for tumor grade stage and margin status assessed through multivariable Cox regression and Kaplan-Meier analyses.	Impact of prostatic ductal adenocarcinoma on biochemical recurrence-free survival outcomes following radical prostatectomy with prostatic acinar adenocarcinoma revealing that the presence of PDA alone does not significantly predict recurrence when controlling for other factors.	Prostatic ductal adenocarcinoma does not independently predict biochemical recurrence-free survival following radical prostatectomy with advanced stage higher tumor grade and positive surgical margins being more significant factors.
Fahad M. Aldakheel, Hadeel Alnajran, Shatha A. Alduraywish et al. 2025Discov Onc	150 individuals analyzed in the study.	Analysis of DNA methylation and transcriptomic signatures to predict prostate cancer recurrence risk.	DNA methylation and transcriptomic signatures in the context of predicting prostate cancer recurrence risk.	Specific DNA methylation and transcriptomic signatures can effectively predict the recurrence risk of prostate cancer.
Johanna Classon, Margherita Zamboni, Camilla Engblom et al. 2022 Molecular Oncology	229 patients with low-intermediate risk prostate cancer and 441 patients with high-risk prostate cancer with specific references to HLA allele carriers across these groups	The intervention from the article is N/A.	Contrasting associations of different HLA alleles with disease recurrence in prostate cancer patients categorized by risk levels indicating significant variations based on HLA type and the presence of CMV immunity.	Specific HLA alleles (notably HLA-A*02:01 and HLA-A*11) and the presence of anti-cytomegalovirus T-cell receptors are significantly associated with the recurrence of prostate cancer post-radical prostatectomy suggesting their potential as biomarkers for disease progression.
Katsuya Hikita, Masashi Honda, Ryutaro Shimizu et al. 2022Asian Journal of Surgery	Involves a sample population of Japanese patients although the exact number of participants is not specified in the citation provided.	Pertains to the timing of the biopsy in relation to surgery specifically robot-assisted radical prostatectomy.	Does not provide a direct comparison; therefore it is categorized as N/A.	Longer time interval between biopsy and surgery is associated with a higher risk of biochemical recurrence after robot-assisted radical prostatectomy in Japanese patients.

Mahendra Singh, Sachin Kathuria, Saurabh Jain et al. 2022 Indian J Surg Oncol	150 male patients who underwent robotic-assisted radical prostatectomy	Robotic-assisted radical prostatectomy.	The article does not provide a specific comparison between different surgical techniques or treatment modalities regarding biochemical recurrence rates.	Specific preoperative parameters significantly correlate with the risk of biochemical recurrence following robotic-assisted radical prostatectomy.
Chao Zhang, Yuying Zhang, Niu et al. 2023 Archivos Españoles de Urología	150 men diagnosed with non-metastatic prostate cancer undergoing radical prostatectomy.	Use of preoperative Prostate Health Index and serum testosterone testing to evaluate the risk of biochemical recurrence after radical prostatectomy in patients with non-metastatic prostate cancer.	Evaluates the predictive capacity of the Prostate Health Index and serum testosterone levels in forecasting biochemical recurrence following radical prostatectomy for non-metastatic prostate cancer.	Preoperative Prostate Health Index and serum testosterone levels can effectively predict biochemical recurrence after radical prostatectomy in patients with non-metastatic prostate cancer.

Patterns and Predictors of Prostate Cancer Recurrence Following Radical Prostatectomy

Recurrence following prostate cancer surgery, particularly radical prostatectomy (RP), represents a significant challenge for oncologists, patients, and researchers alike. This phenomenon is categorized into various types, predominantly comprised of biochemical recurrence (BCR), local recurrence, and distant metastasis. Biochemical recurrence is identified by rising levels of serum prostate-specific antigen (PSA) post-surgery, while local recurrence indicates tumor regrowth within the prostate region, and distant metastasis signifies the spread of cancer to other body parts. Understanding these recurrence types and their underlying mechanisms is essential for developing effective management strategies.

Biochemical recurrence occurs in an estimated 20% to 50% of patients within five to ten years following RP, underscoring the necessity for robust monitoring and treatment plans for this patient population (Siech et al., 2024; (Guo et al., 2024). Mechanistically, post-surgical stress, particularly from prolonged operative times, has been shown to compromise the immune response, thus facilitating the proliferation of residual tumor cells (Meguro et al., 2021). Ahlberg et al. elucidate a predictive aspect wherein the time without PSA recurrence can be an indicator of future outcomes, suggesting that early detection of rising PSA levels is critical for enabling interventions such as salvage therapy (Ahlberg et al., 2022). Consequently, the prompt identification of biochemical recurrence can significantly enhance longitudinal treatment efficacy and patient survival rates.

Salvage therapies, including radiotherapy and hormonal therapy, have become critical in managing biochemical recurrence. Studies indicate that timely interventions post-recurrence can notably improve prognosis. For instance, the efficacy of salvage radiotherapy shows promise, particularly when coupled with androgen deprivation therapy in high-risk patients.

Early applications of these treatments, ideally before PSA levels exceed 0.2 ng/mL, can prevent further systemic disease progression (Cai et al., 2022; Jiang et al., 2023). However, the partnerships between therapy types and recurrence prognostic factors require ongoing exploration to optimize patient outcomes.

Local and distant recurrences further complicate the clinical landscape. Local recurrence can be influenced significantly by positive surgical margins—evidence that cancer cells remain post-surgery (Guo et al., 2024). The presence of positive surgical margins, alongside pathological features like Gleason score and seminal vesicle invasion, are pivotal indicators of high recurrence risk and warrant rigorous clinical follow-up (Guerra et al., 2023; . Additionally, the intersection of local recurrence with advanced detection methods, such as PSMA PET scans, has bolstered efforts to delineate the disease trajectory, providing essential information for future surgical or adjuvant interventions (Mapelli et al., 2023; Jiang et al., 2023).

Risk stratification plays a vital role in predicting recurrence types. Emerging nomograms and clinical scoring systems are designed to refine risk assessments and empower individualized treatment pathways. These tools consider variables such as genetic markers, PSA levels, and specific tumor characteristics, aiming to tailor follow-up surveillance and intervention strategies effectively (Cai et al., 2022; Luo et al., 2022). The integration of genetic profiling into routine practice may offer the capacity to pre-emptively identify patients at high risk of recurrence, thus allowing for accelerated therapeutic approaches and more vigilant monitoring protocols (Li et al., 2022).

The psychological and physical ramifications of recurrence cannot be overlooked, as patients often confront significant stress and anxiety stemming from the prospect of disease relapse. The psychological impact of waiting for PSA results, the uncertainty of disease status, and the implications of potential salvage therapies necessitate a comprehensive approach to patient care that includes mental health support alongside medical treatment (Falagario et al., 2023; Singh et al., 2022). Additionally, the role of patient education regarding recurrence and the importance of adherence to follow-up schedules is paramount to managing treatment outcomes.

Notably, the temporal aspects of recurrence are crucial. Research by Hikita et al. indicates that the interval between initial biopsy and the surgical procedure could have implications for BCR rates, emphasizing the importance of timing in treatment decisions (Hikita et al., 2022). Concurrently, classifying patients based on their Gleason scores and other pathological findings forms part of a robust strategy to mitigate the risk of recurrence by ensuring that the most at-risk patients receive aggressive management strategies promptly (Guerra et al., 2023; Luo et al., 2022).

The complexity of recurrence post-RP hinges on multifactorial influences encompassing surgical techniques, pathological findings, and individual patient characteristics. Professionals involved in the treatment of prostate cancer must remain cognizant of these varied factors and the need for continual dialogue regarding treatment options, surveillance, and emotional support for patients. While significant strides have been made in predicting and managing recurrence post-surgery, ongoing research and clinical trials remain essential to refine strategies and enhance patient prognosis.

Molecular and Genetic Influences of prostate cancer recurrent after radical prostatectomy

Prostate cancer recurrence after radical prostatectomy (RP) is a complex condition influenced by a combination of molecular, genetic, and clinical factors. The recurrence of prostate cancer, typically identified by a rise in prostate-specific antigen (PSA) levels, occurs in approximately 20-40% of men who undergo this surgical intervention. Several studies have explored the predictors of biochemical recurrence (BCR) and have identified various genetic signatures, clinicopathological parameters, and the role of surgical factors, all contributing to the recurrence landscape.

One of the critical factors influencing biochemical recurrence is the presence of positive surgical margins (PSM). According to Guo et al., PSM is associated with increased chances of BCR after RP, as it may indicate residual cancerous tissues left post-surgery, which can result in recurrence (Guo et al., 2024). This notion aligns with findings by Yang et al., demonstrating that PSM significantly correlates with poor outcomes, emphasizing the need for precise surgical techniques to minimize these margins during operation (Yang et al., 2021). Similarly, Bejrananda and Pliensiri found that biochemical recurrence affects approximately 20-30% of individuals post-surgery, underscoring the importance of surgical precision in achieving optimal clinical outcomes (Bejrananda & Pliensiri, 2023).

Genetic factors are emerging as significant predictors of prostate cancer outcomes after RP. The work of Li et al. highlighted that gene signatures related to pyroptosis may predict recurrence more accurately than conventional methods (Li et al., 2022). This complements the findings of Ahlberg et al., which suggest that immediate androgen deprivation therapy could alter survival outcomes based on genetic expression patterns post-recurrence (Ahlberg et al., 2022). Novel genetic frameworks such as those proposed by Cai et al., focusing on lipid metabolism-related genes, further illustrate this evolution towards personalized medicine, indicating distinct metabolic pathways as potential therapeutic targets (Cai et al., 2022).

Factors such as Gleason score and PSA doubling time are critical for risk stratification. The European Association of Urology (EAU) guidelines have underscored the importance of these parameters, linking high Gleason scores with unfavorable prognosis and shorter survival times (Roberts et al., 2022). Elevated PSA levels can be indicative of aggressive disease, with rapid increases potentially warranting immediate intervention. Falagario et al. present findings that stratification based on BCR is linked to mortality risk, highlighting the intersecting nature of biochemical recurrence and overall prognosis in prostate cancer treatment (Falagario et al., 2023).

The role of inflammation and immune response is another pivotal aspect contributing to recurrence patterns. Classon et al. discovered a correlation between certain HLA types and recurrence rates, suggesting that individual immune profiles may influence cancer behavior after surgery (Classon et al., 2022). Such findings pose intriguing questions about how immune modulation might serve as a therapeutic approach in recurrent prostate cancer following RP.

In terms of treatment after recurrence, strategies such as salvage radiotherapy (SRT) have shown promise. Liang et al. emphasized that combining SRT with endocrine therapy could enhance treatment efficacy in patients experiencing BCR, suggesting a multi-faceted

approach to management post-surgery (Liang et al., 2023). However, not all patients respond to these interventions; thus, further research is warranted to tailor treatment protocols based on individual risk profiles, emphasizing the necessity for personalized care strategies.

Psychosocial factors also play a critical role in post-operative outcomes. Age, body mass index (BMI), and general health are associated with biochemical recurrence, as highlighted by Siech et al., pointing to the need for comprehensive patient assessments beyond just clinical and genetic indicators (Siech et al., 2024). Health-related quality of life and psychological impacts can significantly affect prognosis and treatment adherence, demanding a more holistic approach to patient management.

Advances in diagnostic imaging, particularly PET scans utilizing PSMA, are proving instrumental in the early detection of recurrent disease, allowing timely therapeutic interventions (Jiang et al., 2023). Studies have shown that earlier identification of recurrence through advanced imaging correlates with improved treatment outcomes, underscoring technology's role in modern oncology.

As the field of prostate cancer treatment evolves, key aspects such as genetic profiling, surgical techniques, and patient-centered care will play an increasingly vital role in managing recurrence rates after radical prostatectomy. Continuous research into the molecular mechanisms underlying prostate cancer recurrence will be essential for developing predictive models that enhance treatment protocols and improve patient prognoses.

The recurrence of prostate cancer following radical prostatectomy is influenced by a myriad of factors, including molecular markers, surgical outcomes, genetic predispositions, and patient characteristics. By integrating these diverse aspects, clinicians can better forecast recurrence risks and tailor treatment strategies to improve patient outcomes. Further investigation into genetic signatures, immune response profiles, and technological advancements in detection will be crucial in the ongoing fight against this prevalent malignancy.

Strength and limitations

This study provides a comprehensive overview of current evidence on the causes of prostate cancer recurrence after radical prostatectomy by synthesizing findings from multiple clinical studies and case reports within the last five years. The strength of this review lies in its systematic search strategy, focused inclusion criteria, and evaluation of both surgical and molecular predictors of recurrence. However, the study is limited by its reliance on retrospective reports, potential publication bias, and variability in study populations and follow-up durations across included articles.

CONCLUSION

This study concludes that prostate cancer recurrence after radical prostatectomy is a multifactorial issue influenced by positive surgical margins, tumor aggressiveness, genetic markers, surgical technique, and patient-specific variables. Early identification of recurrence, particularly biochemical recurrence, is critical for initiating salvage treatments that improve long-term outcomes. Future studies should focus on refining predictive models and integrating genetic profiling and imaging technologies to personalize management strategies for high-risk patients. All research contributors, if any, should be listed briefly in the text before the references.

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