

Late Vertebral Metastasis in Long-Term Survivors of Breast, Prostate, and Renal Cell Cancer

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Received date: September 28, 2026, **Accepted date:** October 07, 2026 **Published date:** October 14, 2026.

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Abstract

Long-term survivors of hormone receptor-positive breast cancer, prostate adenocarcinoma, and renal cell carcinoma may develop metastatic disease years after apparently successful treatment. Vertebral involvement can cause pain, instability, and neurologic injury, but the incidence of first late vertebral recurrence is poorly measured because survivorship cohorts commonly report bone metastases without identifying vertebral events.

This narrative review separates late first distant recurrence from progression of established metastatic disease; summarizes tumor-specific clinical and biological evidence; and considers how suspected vertebral disease should be evaluated. Persistent distant-recurrence risk is well established for estrogen

receptor-positive breast cancer, whereas evidence for delayed vertebral recurrence in prostate and renal cell cancer is more heterogeneous. Proposed marrow-dormancy mechanisms derive largely from experimental or nonvertebral bone studies.

Routine spine MRI of asymptomatic survivors has no established benefit. In a distinct population with known spinal metastases and castration-resistant prostate cancer, a randomized screening trial did not significantly reduce clinical cord compression. Clinical vigilance should instead focus on timely evaluation of concerning symptoms and tumor-specific evidence of recurrence, followed by multidisciplinary assessment of neurologic compression, mechanical stability, oncologic options, and systemic status. Prospective cohorts with vertebral-specific endpoints are needed before risk-adapted screening can be recommended.

Keywords

vertebral metastasis; cancer survivorship; late recurrence; spinal cord compression; narrative review

Introduction

Late distant recurrence remains a concern after curative-intent treatment for several solid tumors. Estrogen receptor–positive breast cancer has a sustained risk of distant recurrence for at least two decades; renal cell carcinoma (RCC) can recur after prolonged disease-free intervals; and prostate cancer can be detected years after definitive local treatment during evaluation of biochemical recurrence. [1–4] Yet “bone recurrence” is rarely reported at vertebral-level resolution. A late first vertebral metastasis is therefore difficult to quantify, despite its potential consequences for pain, stability, and neurologic function.

The clinical question is not whether every survivor should undergo spine imaging. It is which presentations merit prompt diagnostic attention, what spine-specific decisions follow detection, and which evidence gaps prevent a validated screening strategy. This review compares three malignancies with recognized delayed skeletal involvement and explicitly distinguishes first late recurrence from oligoprogression of established metastatic disease.

Methods and Definitions

This narrative review integrates clinical, epidemiologic, and biological literature rather than attempting a quantitative synthesis. A focused search of PubMed/MEDLINE, Embase, and Web of Science for English-language publications from 1990 through January 2025 was described in the initial manuscript, with additional sources identified through citation chaining. A targeted update for this revision identified selected clinical studies and guidance available through

September 2026. Sources were selected for relevance to latency, vertebral events, imaging, and clinical decisions. No exhaustive screening, formal risk-of-bias assessment, or pooled incidence estimate was undertaken.

For this review, late first recurrence means a new distant metastatic diagnosis more than 5 years after curative-intent treatment in a patient without previously recognized distant disease; recurrence more than 10 years later is described as very late. Biochemical recurrence is an abnormal tumor marker after local therapy and is not synonymous with radiologically confirmed metastasis. Oligoprogression denotes progression at a limited number of sites in a patient with established metastatic disease receiving systemic treatment. These entities should not share a single incidence denominator.

What Is Known About Late Vertebral Recurrence

Hormone receptor–positive breast cancer

The strongest long-term population evidence concerns estrogen receptor–positive breast cancer. An individual-patient meta-analysis found continuing distant-recurrence risk between years 5 and 20 after 5 years of endocrine therapy, with substantial variation by original tumor size and nodal status.[1] Bone is a common site of breast cancer relapse, but the cited long-term recurrence data do not establish the incidence, timing, or first-site status of vertebral metastasis. The review should therefore use these data to establish prolonged systemic risk, not a spine-specific rate.

Prostate adenocarcinoma

After prostatectomy or radiotherapy, late biochemical recurrence may trigger staging, including prostate-specific membrane antigen (PSMA) PET imaging. PSMA PET can localize recurrent disease at low prostate-specific antigen levels, but a positive vertebral

focus requires correlation with anatomic imaging and clinical context.[4] Trials of metastasis-directed therapy in oligometastatic prostate cancer inform management of selected patients with detected lesions; they do not establish a benefit from routine spine MRI in asymptomatic, disease-free survivors.[5] First metastatic recurrence, known asymptomatic spinal metastases, and castration-resistant oligoprogression should be discussed as separate clinical settings.

Renal cell carcinoma

RCC may recur after a long disease-free interval following nephrectomy. Late-recurrence series and case reports support biological possibility, but estimates depend strongly on the stage and histology of the original tumor, length of follow-up, and whether the denominator is all nephrectomy patients, long-term survivors, or patients who recurred. [2,3] Vertebral RCC metastases can be destructive and vascular, yet a reliable rate of vertebra as the first site of very late recurrence is not established by the sources reviewed. A claim that the spine “frequently” represents the initial site should be avoided.

Biological Plausibility and Its Limits

Vertebral marrow is a plausible site of disseminated tumor-cell persistence. Venous and arterial routes can deliver tumor cells to the axial skeleton, and endosteal and perivascular niches have been implicated in dormancy and reactivation. [6–8] Breast cancer models implicate marrow-niche interactions; prostate cancer bone metastasis involves tumor–osteoblast signaling; and clear-cell RCC biology includes hypoxia-inducible signaling and angiogenesis. [7–10] These mechanisms support a rationale for studying delayed skeletal relapse. They do not demonstrate a unique vertebral dormancy program or prove that a new late lesion arose from a continuously quiescent vertebral cell. Studies of myeloma or nonvertebral metastases should be

described as indirect evidence when applied to late vertebral relapse.

The Surveillance Question

Routine spinal screening in asymptomatic survivors has no validated interval, risk threshold, or patient-centered outcome benefit. The most directly relevant randomized test of spinal MRI screening concerned a different population: 420 patients with metastatic castration-resistant prostate cancer and known asymptomatic spinal metastases.

In PROMPTS, screening detected radiological cord compression in 61 of 200 assessable scans, but clinical cord compression at 1 year was 6.7% in the control group and 4.3% in the screening group; the time-to-event comparison was not statistically significant (hazard ratio 0.64, 95% CI 0.37–1.11). [11] Its findings cannot be extrapolated directly to long-term disease-free survivors, but they caution against assuming that detection of subclinical abnormalities necessarily prevents clinically meaningful events.

Guidance for people with known spinal metastases likewise advises against MRI solely for early radiological detection of cord compression when symptoms or signs are absent. [12] Conversely, a past or current cancer diagnosis combined with concerning pain or neurologic symptoms warrants prompt assessment; suspected metastatic spinal cord compression requires urgent MRI and specialist coordination.[12]

Tumor-directed imaging at biochemical recurrence is a separate indication from scheduled spine screening. Incidental vertebral findings may lead to false positives, biopsy, repeated imaging, cost, and anxiety; these outcomes must be measured in future studies.

A phase II trial suggested fewer skeletal-related events with prophylactic radiotherapy for selected high-risk

asymptomatic bone metastases, but it studied patients with established metastatic cancer and an intervention after lesions were already identified. [13] It does not establish a screening policy for survivors without known metastases.

Evaluation After a Vertebral Lesion Is Suspected or Detected

The practical contribution for spine care begins at recognition of possible vertebral disease (Figure 1). New or progressive back pain, mechanical pain, radicular symptoms, weakness, gait change, and sphincter dysfunction require assessment proportionate to the concern for spinal metastasis or cord compression. Suspected cord compression is an urgent pathway rather than a routine surveillance decision.[12]

Imaging should define the involved levels, epidural extent, and structural integrity, while systemic staging and tissue confirmation are individualized according to known cancer history and diagnostic uncertainty.

Once a lesion is identified, multidisciplinary evaluation can be organized around the neurologic, oncologic, mechanical, and systemic (NOMS) domains.[14] The neurologic domain includes symptoms and epidural spinal cord compression; the mechanical domain includes pain and stability, for which the Spinal Instability Neoplastic Score provides a common language. [15]

Histology, prior radiation, systemic therapy options, expected survival, and patient goals affect the balance among radiation, stabilization, decompression, and other care. A newly detected lesion does not automatically require surgery or stereotactic radiotherapy.

Research Priorities

Prospective survivorship cohorts should record the date

and site of first distant recurrence at vertebral-level resolution, distinguish new metastasis from progression of established disease, and capture the imaging indication. Endpoints should include neurologic function, instability or fracture, unplanned surgery, treatment burden, quality of life, false-positive workups, and cost. Risk models should account for primary stage, biology, treatment exposure, time since treatment, and competing mortality. Only after an enriched population and actionable detection window are identified should a randomized strategy compare risk-adapted imaging with current clinical evaluation.

Limitations

This selective narrative synthesis cannot estimate the incidence of late first vertebral recurrence or establish comparative screening effectiveness. Several tumor-specific mechanisms derive from experimental bone models rather than direct studies of human vertebral marrow. Literature across localized survivorship and advanced metastatic disease is heterogeneous, and results from one setting must not be transferred to another without qualification.

Conclusions

Late vertebral metastasis is a consequential possibility after breast, prostate, or renal cell cancer, but its incidence as a first late metastatic event remains poorly defined. Current evidence does not justify scheduled spine MRI for asymptomatic long-term survivors. Concerning symptoms and tumor-specific evidence of recurrence warrant timely diagnostic evaluation; when a vertebral lesion is found, neurologic compression, mechanical stability, oncologic options, and systemic status guide care. Vertebral-specific prospective data are needed to determine whether any risk-defined detection strategy improves outcomes.

Feature	HR-positive breast cancer	Prostate adenocarcinoma	Renal cell carcinoma
Late-recurrence evidence	Distant-recurrence risk persists through 20 years; vertebral timing incompletely reported.[1]	Late biochemical or metastatic recurrence can follow local therapy; marker relapse is not vertebral relapse.[4]	Recurrence can occur >10 years after nephrectomy; estimates vary by cohort. [2,3]
Vertebral-specific evidence	Often combined with other bone sites in survivorship datasets.	Spinal lesions can be found during recurrence staging; few survivorship cohorts report first vertebral events.	Late vertebral lesions are described, but first-site incidence is uncertain.
Typical lesion phenotype	Often lytic or mixed.	Often sclerotic, though mixed and lytic lesions occur.	Often lytic and potentially hypervascular.
Proposed bone mechanisms	Marrow niche and endocrine signaling. [7,8]	Tumor-osteoblast signaling.[9]	Hypoxia and angiogenic pathways.[10]
Common clinical trigger	Concerning symptoms or tumor-directed staging.	PSA rise and tumor-directed staging; symptoms require separate assessment.	Concerning symptoms or findings on scheduled tumor follow-up.
Spine-care implication	Assess concerning pain or neurologic change promptly.	Do not equate PSMA uptake with instability or epidural disease.	Assess stability and vascularity when treating an identified lesion.

HR = hormone receptor; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen. Entries distinguish evidence for late systemic recurrence from evidence for late first vertebral recurrence. They do not constitute screening recommendations.

Table 1: Late recurrence and vertebral considerations across selected malignancies

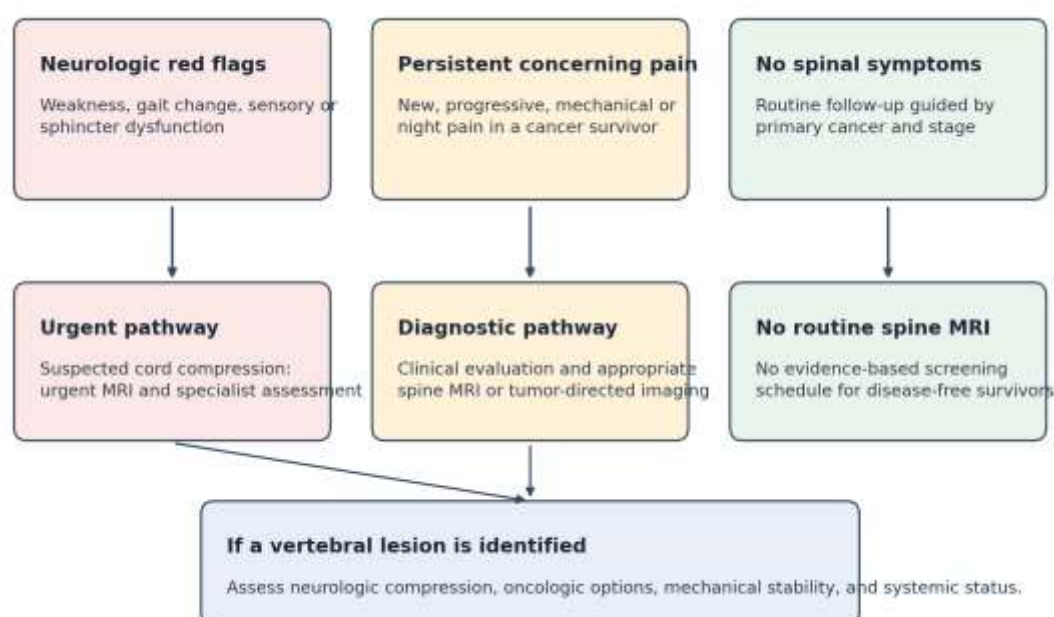


Figure 1: Clinical pathways for possible vertebral metastasis

Conceptual decision pathway for a survivor of solid cancer. Urgency depends on symptoms and examination. Tumor-specific recurrence staging and evaluation of a suspected vertebral lesion are distinct from screening an asymptomatic survivor. The figure is not a validated risk algorithm.

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