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Hip prosthetic loosening and periprosthetic osteolysis: A commentary

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Abstract

Prosthetic loosening and periprosthetic osteolysis have been debated for decades, both in terms of the timing and nature of the triggering events. The hypothesis of wear-particle-induced loosening states that wear particles cause a foreign-body response leading to periprosthetic osteolysis and ultimately to late prosthetic loosening, *i.e.*, that the osteolysis precedes the loosening. The theory of early loosening, on the other hand, postulates that the loosening is already initiated during or shortly after surgery, *i.e.*, that the osteolysis is secondary to the loosening. This commentary focuses on the causal relationship between prosthetic loosening and periprosthetic osteolysis.

Key Words: Hip prosthesis; Radiostereometric analysis; Prosthesis failure; Osteoclasts; Bone resorption; Alarmins

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Core Tip: Prosthetic loosening and periprosthetic osteolysis have been debated for decades. Some authors claim that the osteolysis precedes the loosening, others that the osteolysis is secondary to the loosening. This commentary focuses on their causal relationship.

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INTRODUCTION

Hip arthroplasty is one of the most successful of all orthopedic operations, but the

results do deteriorate with time due to loosening. In the 1970s, the hypothesis of wear-particle-induced loosening, later called particle disease, was proposed: It was assumed that wear particles cause a foreign-body response leading to periprosthetic osteolysis and ultimately to late prosthetic loosening. Wear particles are still widely considered to be the main cause of loosening[1-4]. However, there is much evidence that loosening is already initiated during or shortly after surgery (due to insufficient initial fixation or resorption of a necrotic bone bed) and that the prosthetic micromovements then cause devitalizing periprosthetic fluid pressure fluctuations leading to periprosthetic osteolysis[5-9]. This commentary focuses on the causal relationship between prosthetic loosening and periprosthetic osteolysis.

WEAR PARTICLES *PER SE* DO NOT INDUCE OSTEOLYSIS

The hypothesis of wear-particle-induced loosening presupposes that wear particles are somehow transported into the interface between bone and prosthesis and once there, trigger a foreign-body response leading to periprosthetic osteolysis (and ultimately to prosthetic loosening). However, histological studies indicate that a stable implant has a biological barrier that prevents wear particles from entering into the bone-prosthetic interface[10,11]. Even if the biological barrier were defective, experiments have shown that *uncontaminated* particles (if very gently deposited between the bone surface and a stable implant) do not induce osteolysis[12,13]. Thus, wear particles *per se* appear not to induce osteolysis.

ENDOTOXINS AND DAMPS CAN INDUCE OSTEOLYSIS

Wear particles contaminated by endotoxins can induce transient osteolysis[14,15], but it has been experimentally shown that endotoxins are rapidly eliminated or inactivated[13]. By contrast, prosthetic micromovements of *loosened* prosthetic components can cause sustained, devitalizing spikes of high fluid pressure in the bone-implant interface, which can lead to progressive periprosthetic osteolysis[5-9]. The molecular mechanism appears to be that necrotic osteocytes release DAMPs (damage-associated molecular patterns, danger signals, or alarmins)[16], which, *via* a unique pattern recognition receptor, reinforce osteoclastogenesis[17]. DAMPs, released due to prosthetic loosening, may, therefore, (unlike endotoxins) induce sustained excessive osteoclast activity and thus cause progressive periprosthetic osteolysis.

DAMPs-COATED PARTICLES CAN INHIBIT BONE INGROWTH

A series of animal experiments with polyethylene particles inserted into the interface between the bone and a movable part of a previously installed implant have shown inhibition of bone ingrowth only when combined with movements at the interface, *i.e.* no inhibition occurred at a stable interface. Remarkably, after the movements ceased, the inhibition of bone ingrowth persisted if particles were present, while no inhibition occurred in the control group without particles[12].

A plausible explanation of the persistent inhibition of bone ingrowth after the movements ceased is that the movements caused the release of DAMPs, that adhered to the polyethylene particles at the interface, thus forming DAMPs-coated bone-formation-inhibiting polyethylene particles. Varying degrees of DAMPs-coating may actually explain why different authors have come to very different conclusions about the importance of the material and size of the wear particles in loosening (a significant foreign-body response to particles of cement, metal, and polyethylene have been reported, but also no or almost no response)[18]. A similar mechanism (DAMPs-coated particles) for osteolysis may also apply to experimental models exposed to both surgical trauma and wear particles.

UNCEMENTED PROSTHETIC COMPONENTS DO NOT FORM DAMPs-COATED CEMENT PARTICLES

Radiostereometric analysis (RSA) enables highly accurate *in vivo* measurements of the prosthetic component migration after surgery. Many RSA studies of hip prostheses have shown that early migration poses a risk of future failure – the larger the early migration, the greater the risk of future failure[19-24]. However, some RSA studies indicate that certain uncemented femoral components appear to achieve stability and possibly even osseointegration during the healing period despite significant early migration[25-27].

If, as suggested in these studies, these uncemented femoral components (unlike cemented femoral components with similar significant early migration) really become osseointegrated during the healing period, a probable explanation is that no DAMPs-coated cement particles, which could inhibit bone ingrowth and thereby prevent osseointegration, have been formed.

CONCLUSION

The recent clarification of the molecular mechanism behind osteoclastogenesis (the pattern recognition receptor to osteocyte-derived DAMPs)[17] allows us to better understand the causal relationship between prosthetic loosening and periprosthetic osteolysis: Loosening is initiated during or shortly after surgery (due to insufficient initial fixation or resorption of a necrotic bone bed). The micromovements of thus loosened prosthetic components may, *via* periprosthetic fluid pressure fluctuations, cause necrotic osteocytes, which release DAMPs that reinforce the osteoclast activity and lead to periprosthetic osteolysis. Later and *secondary to loosening*, DAMPs-coated wear particles may be formed, which, by inhibiting bone ingrowth, may affect the progression of loosening.

FOOTNOTES

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