



Orthopaedics and diabetes

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With about 12% of orthopaedic patients being diabetic and a large proportion of them being obese as well, orthopaedic surgeons are commonly involved in managing diabetic patients in both outpatient and inpatient setting. This review summarizes current concepts in diabetes management including specific orthopaedic issues and future directions of diabetes management.

Keywords : diabetes ; orthopaedics ; surgery.

INTRODUCTION

The estimated global prevalence of diabetes in 2011 was 366 million ; it was expected to rise to 552 million by 2030. It is estimated that more than 1 in 20 in the United Kingdom suffer from diabetes (diagnosed and undiagnosed). In 2011, there were 2.9 million diagnosed with diabetes in UK ; the average prevalence in UK is 4.45%. Ten percent of adults with diabetes have Type 1 diabetes and 90% have Type 2. Apart from genetic and ethnic factors, obesity appears to be the most potent risk factor for diabetes. It accounts for 80-85% risk of developing Type 2 diabetes and appears to be responsible for the global epidemic. Almost two in every three people in the UK are estimated to be obese. Individuals with diabetes account for 15-16% of deaths in England. The direct and indirect costs associated with diabetes management in UK currently stands at £23.7 billion per annum (3).

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Musculoskeletal conditions account for around 12% of all general practitioner consultations in the UK (15). Diabetic patients have a much higher prevalence of musculoskeletal problems ; a study showed as much as 82% in a pilot cohort of 208 Type 2 diabetic patients (5).

Orthopaedic problems in diabetic patients

Diabetic patients may present with any orthopaedic condition or trauma or with infections. Prevalence of diabetes in elective orthopaedic setting such as joint replacement was found to be around 12% in a group of 874 patients (28) and average BMI (Body Mass Index) of these patients was over 30. These patients have been shown to have significantly increased risk of complications such as surgical site infections in a retrospective study of 7181 primary arthroplasties (14). Obese diabetic patients were found to have the highest risk of developing deep infection in a prospective study of 1214 consecutive knee replacements (6).

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Diabetes mellitus adversely affects the skeleton and increases risk of osteoporosis and fragility fractures. The mechanisms underlying low bone strength are not fully understood but may be due to low peak bone mass attained and the effect of diabetic complications, such as nephropathy (12). Patients with Type 2 Diabetes have increased fracture risk either inherent or as a result of their medications and their effect on bone mass (11). Review articles on diabetic ankle fractures quote a much higher rate of complications compared to similar fractures in non-diabetics and the risk increases in patients with co-existing neuropathy (1). Life time risk of diabetic patients developing a foot ulcer is as high as 25% (25) thereby putting them in potential danger of an amputation. Peripheral neuropathy affects between 30-50% of people with diabetes and increases risk of heel ulceration, particularly if peripheral vascular disease is also present (10).

Diabetes leads to increased morbidity and increased length of stay, thereby increasing inpatient costs. Optimal management of diabetes in surgical patient seems to play an important role in both preventing complications and reducing costs associated with treatment.

Diabetes and Trauma

Trauma is known to cause hyperglycaemia (16) by stress induced catabolic hormone secretion. Stress induced hyperglycaemia has been shown to increase mortality risk in trauma patients to an extent greater than in diabetics with hyperglycaemia in a study involving 5117 trauma patients (16). Early hyperglycaemia with glucose levels greater than 200 mg/dL has been shown to be highly predictive of higher infection and mortality rates in 516 trauma patients admitted to intensive care unit, independent of other injury characteristics, confirming need for tight control of blood glucose levels (17). Intensive insulin therapy is widely practiced to achieve tight glycaemic control in critically ill trauma patients with diabetes (and with stress induced hyperglycaemia) to improve outcome even though comparative studies show no evidence to suggest that it decreases mortality (26).

Management of Diabetes during surgery

Glycaemic control has a significant impact on the risk of post-operative infection. As much as 25% diabetic surgical patients experience a hypoglycaemic episode (22). Diabetic ketoacidosis is an avoidable complication in the post-surgical patient.

Factors leading to adverse outcome in diabetic surgical patients include failure to identify or diagnose, non-adherence to existing guidelines, lack of knowledge among staff and prescribing errors (22).

With increasing prevalence of diabetes in surgical patients, the challenges faced also include higher proportion of associated co-morbidities, prolonged length of stay, increasing patient demands.

Surgery causes metabolic stress and catabolic hormone secretion induces transient hyperglycaemia. Starvation adds to this metabolic stress. Post operatively there is a period of insulin resistance causing a period of functional insulin insufficiency. Diabetic patients are unable to respond to this increased demand for insulin. Even in the absence of diabetes, transient hyperglycaemia in the peri-operative period has been shown to be an important risk factor in post-operative infection in a retrospective comparative study of 790 orthopaedic patients (24).

Management of diabetes in peri-operative period includes management at pre-operative assessment, at the time of surgery, post-operative care and after discharge.

Diabetes management is largely carried out in primary care setting and optimal management of diabetes is important before considering elective surgery. Along with maintaining an optimal HbA1c level, management of related co-morbidities and identification of diabetic complications are equally important.

Early referral to diabetic specialist team should be considered in any patient in whom diabetes control is found to be suboptimal during pre-operative assessment. High risk patients such as ones with poor glycaemic control or associated complications should be identified early. An individualized diabetes management plan is recommended for each patient. Prolonged starvation is to be avoided

and ideally patients should not be on an evening list (2).

Variable rate intravenous insulin infusion (VRIII – previously known as sliding scale) may be avoided in patients who are likely to starve only for short periods such as one missed meal. Blood sugar should be checked regularly especially when the patient is sleeping or under sedation so that hypoglycaemia does not go undetected. The aim is to maintain capillary blood glucose level between 6-10 mmol/L. Local guidelines should be adhered to regarding peri-operative diabetes management and the diabetes team should be consulted when in doubt. Fluid management is equally important especially when the patient is on VRIII and the aim is to maintain glucose and electrolytes along with intravascular volume. Most patients who undergo emergency surgery such as trauma patients are likely to need VRIII peri-operatively followed by subcutaneous insulin during the post-operative period to ensure prompt glycaemic control. Insulin has been labelled as one of the highest risk medications in the inpatient setting (13). Safe prescribing and administering practices should be followed in order to reduce this risk.

During surgery along with ensuring glycaemic, electrolyte and fluid balance, attention should be paid to avoiding pressure damage to feet. Blood glucose should be monitored at least hourly and maintained at 6-10 mmol/L. If glucose level is not stable, it may need to be monitored more frequently. VRIII is to be considered only if blood glucose cannot be maintained below 12 mmol/L with regular insulin. Use of anaesthetic techniques to reduce post-operative nausea and vomiting is encouraged so that early return to normal diet and normal diabetes treatment can be facilitated. Regional and local anaesthetic techniques help in achieving this. In the post-operative period an early return to normal diet and diabetes self-management by patient are encouraged. Special care should be taken of feet during the recovery period, especially when regional anaesthetic techniques have been used and the patient is unable to move. Discharge planning should include considerations to factors such as patients social and care setting and ability to self-manage diabetes while at their usual residence. A

blood glucose monitoring and treatment plan should be agreed to before safe discharge (2).

Infections

Diabetic foot infections usually start as superficial skin ulceration (18). In 25% of these, infection may spread to deeper tissues or to bone. Ten to thirty percent of patients with a foot ulcer eventually end up with an amputation (8). Impaired immunologic disturbances which predispose diabetics to foot infections may be correlated with poor glycaemic control (18). Vascular insufficiency and peripheral neuropathy lead to poor healing of diabetic foot ulcers, rendering them vulnerable to spreading to deeper structures. Acute infections may be caused by aerobic Gram positive cocci but chronic infections have mixed flora, thereby making accurate microbiological diagnosis and antibiotic management difficult. Sample taken by curettage from the base of the ulcer has been shown to give more reliable diagnosis than a simple wound swab in a study of 54 patients (21). Along with *Staphylococcus aureus*, Gram negative bacilli and anaerobes are frequently isolated from the deep tissue samples. Antibiotic-resistant organisms, such as methicillin-resistant *S. Aureus*, are frequently isolated from patients who have previously received antibiotic therapy especially after repeated hospitalizations.

Clinical picture may be misleading and may not show signs of sepsis in long standing infections. Inflammatory markers such as CRP (C Reactive Protein) have been found to be more reliable than clinical picture in monitoring diabetic foot infections in prospective studies (7). Osteomyelitis may be looked for clinically by bone probing but this has been shown to have poor inter-observer reliability in a cross-sectional study of 75 patients with diabetic foot ulcer (9). MRI (Magnetic Resonance Imaging) appears to be the currently accepted investigation of choice in detecting osteomyelitis in comparison with conventional radiographs, bone scan or leukoscans (4). Diabetic feet should be managed by multi-disciplinary teams including surgeons, diabetic specialists, podiatrists, physiotherapists and nurses. This has been shown to influence the overall outcome such as reducing major amputations (31).

Newer Anti-diabetic agents and their implications in orthopaedic practice

Type 1 Diabetes is managed mostly with Insulin as either a Basal Bolus Regime or Twice Daily Mixed Insulin or Continuous Subcutaneous Insulin Infusion. The initial emphasis in the obese Type 2 Diabetes patients would be to reduce the insulin resistance. This is most commonly attempted by starting the patient on Metformin. Metformin reduces the risk of microvascular complications by about 30% (27). Metformin also helps in weight reduction. Metformin has also been shown to enhance osteoblasts differentiation and inhibit osteoclast differentiation *in vitro* and prevent bone loss in laboratory animals (19). This has not been proven to show beneficial effects in humans yet. Sulphonylureas like gliclazide are insulin secretagogues and directly stimulate the pancreas to produce insulin. Metformin and sulphonylureas may counter the harmful bone effects of diabetes, as risk of fracture in patients treated with these drugs seems to be reduced compared with the general population (23). Further studies are needed to elucidate mechanisms of action by which metformin and sulphonylureas may affect bone.

Thiazolidinediones such as Pioglitazone are commonly used to reduce insulin resistance. These cause weight gain. They have been shown to induce bone loss and cause secondary osteoporosis, again not proven by clinical studies (11). In patients who have been on these medications especially women who may have sustained fractures, it may be advisable to monitor Bone mineral density (BMD). However recent evidence suggests that BMD may not be sensitive enough to measure fracture risk in these patients but no definitive solution has been found yet (30). These should definitely be avoided in osteoporotic or osteopenic patients.

Newer diabetic medications such as GLP-1 (glucagon like peptide-1) analogues have been shown to offer protective effect on bone metabolism (29) but again clinical studies will be needed to prove their beneficial effects. Similarly DPP4 Inhibitors (Dipeptidyl peptidase-4 inhibitors) have been shown to reduce risk of fractures in randomised controlled trials (20). These may also help in weight

loss in obese Type 2 diabetics ; thereby reducing their risk of complications following orthopaedic interventions.

CONCLUSIONS

Diabetic patients have a high prevalence of orthopaedic problems and also have increased risk of complications following orthopaedic interventions. Identification of patients at risk is vital in preventing these complications. Careful management of blood glucose level is warranted during any surgical procedure and advice may be sought from Diabetic specialist team if necessary. Diabetic patients are at risk of osteoporosis and careful monitoring of bone mineral density and avoidance of drugs such as Thiazolidinediones may help in prevention of fractures in this vulnerable group.

REFERENCES

1. Chaudhary SB, Liporace FA, Gandhi A *et al.* Complications of ankle fracture in patients with diabetes. *J Am Acad Orthop Surg* 2008 ; 16 : 159-170.
2. Dhataria K, Flanagan D, Hilton L *et al.* Management of adults with diabetes undergoing surgery and elective procedures : improving standards. 2011. <http://www.diabetes.nhs.uk/document.php?o=224> .
3. Diabetes UK. 2012. <http://www.diabetes.org.uk/Documents/Reports/Diabetes-in-the-UK-2012.pdf>
4. Donovan A, Schweitzer ME. Current concepts in imaging diabetic pedal osteomyelitis. *Radiol Clin North Am* 2008 ; 46 : 1105-1124, vii.
5. Douloumpakas I, Pырpasopoulou A, Triantafyllou A, Sampanis C, Aslanidis S. Prevalence of musculoskeletal disorders in patients with type 2 diabetes mellitus : a pilot study. *Hippokratia* 2007 ; 11 : 216-218.
6. Dowsey MM, Choong PF. Obese diabetic patients are at substantial risk for deep infection after primary TKA. *Clin Orthop Relat Res* 2009 ; 467 : 1577-1581.
7. Dzieciuchowicz Ł, Kruszyna Ł, Krasieński Z, Espinosa G. Monitoring of systemic inflammatory response in diabetic patients with deep foot infection treated with negative pressure wound therapy. *Foot Ankle Int* 2012 ; 33 : 832-837.
8. Edmonds M. Modern treatment of infection and ischaemia to reduce major amputation in the diabetic foot. *Curr Pharm Des* 2013 ; 9 ; 5008-5015.
9. García Morales E, Lázaro-Martínez JL, Aragón-Sánchez FJ *et al.* Inter-observer reproducibility of probing to bone in the diagnosis of diabetic foot osteomyelitis. *Diabet Med* 2011 ; 28 : 1238-1240.

10. **Gordois A, Scuffham P, Shearer A, Oglesby A, Tobian JA.** The health care costs of diabetic peripheral neuropathy in the US. *Diabetes Care* 2003 ; 26 : 1790-1795.
11. **Grey A.** Thiazolidinedione-induced skeletal fragility-mechanisms and implications. *Diabetes Obes Metab* 2009 ; 11 : 275-284.
12. **Hamann C, Kirschner S, Günther KP, Hofbauer LC.** Bone, sweet bone - osteoporotic fractures in diabetes mellitus. *Nat Rev Endocrinol* 2012 ; 17 ; 8 : 297-305.
13. **Hellman R.** A systems approach to reducing errors in insulin therapy in the inpatient setting. *Endocr Pract* 2004 ; 10 : 100-108.
14. **Jämsen E, Nevalainen P, Eskelinen A et al.** Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection : a single-center analysis of 7181 primary hip and knee replacements for osteoarthritis. *J Bone Joint Surg* 2012 ; 94-A : e101. doi : 10.2106/JBJS.J.01935.
15. **Jordan K, Clarke AM, Symmons DP et al.** Measuring disease prevalence : a comparison of musculoskeletal disease using four general practice consultation databases. *Br J Gen Pract* 2007 ; 57 : 7-14.
16. **Kerby JD, Griffin RL, MacLennan P, Rue LW 3rd.** Stress-induced hyperglycemia, not diabetic hyperglycemia, is associated with higher mortality in trauma. *Ann Surg* 2012 ; 256 : 446-452.
17. **Laird AM, Miller PR, Kilgo PD, Meredith JW, Chang MC.** Relationship of early hyperglycemia to mortality in trauma patients. *J Trauma* 2004 ; 56 : 1058-1062.
18. **Lipsky BA, Berendt AR, Deery HG et al. Infectious Diseases Society of America.** Diagnosis and treatment of diabetic foot infections. *Plast Reconstr Surg* 2006 ; 117 (7 Suppl) : 212S-238S.
19. **Mai QG, Zhang ZM, Xu S et al.** Metformin stimulates osteoprotegerin and reduces RANKL expression in osteoblasts and ovariectomized rats. *J Cell Biochem* 2011 ; 112 : 2902-2909.
20. **Monami M, Dicembrini I, Antenore A, Mannucci E.** Dipeptidyl peptidase-4 inhibitors and bone fractures : a meta-analysis of randomized clinical trials. *Diabetes Care* 2011 ; 34 : 2474-2476.
21. **Mutluoglu M, Uzun G, Turhan V et al.** How reliable are cultures of specimens from superficial swabs compared with those of deep tissue in patients with diabetic foot ulcers ? *J Diabetes Complications* 2012 ; 26 : 225-229.
22. **Rayman G.** Inpatient audit. *Diabetes Update*. 2010. http://www.diabetes.org.uk/upload/Professionals/Publications/Comment_Inpatient%20audit_new.pdf
23. **Rejnmark L.** Bone effects of glitazones and other anti-diabetic drugs. *Curr Drug Saf* 2008 ; 3 : 194-198.
24. **Richards JE, Kauffmann RM, Zuckerman SL, Obremskey WT, May AK.** Relationship of hyperglycemia and surgical-site infection in orthopaedic surgery. *J Bone Joint Surg* 2012 ; 94-A : 1181-1186.
25. **Richard JL, Schuldiner S.** Epidemiology of diabetic foot problems. *Rev Med Interne* 2008 ; 29 Suppl 2 : S222-S230.
26. **Treggiari MM, Karir V, Yanez ND, Weiss NS, Daniel S, Deem SA.** Intensive insulin therapy and mortality in critically ill patients. *Crit Care* 2008 ; 12 : R29.
27. **Viollet B, Guigas B, Sanz Garcia N et al.** Cellular and molecular mechanisms of metformin : an overview. *Clin Sci (Lond)* 2012 ; 122 : 253-270.
28. **Warth LC, Callaghan JJ, Wells CW et al.** Demographic and comorbid disparities based on payer type in a total joint arthroplasty cohort : implications in a changing health care arena. *Iowa Orthop J* 2011 ; 31 : 64-68.
29. **Walsh JS, Henriksen DB.** Feeding and bone. *Arch Biochem Biophys* 2010 ; 503 : 11-19.
30. **Yamaguchi T.** Bone fragility in type 2 diabetes mellitus. *World J Orthop* 2010 ; 1 : 3-9.
31. **Yesil S, Akinci B, Bayraktar F et al.** Reduction of major amputations after starting a multidisciplinary diabetic foot care team : single centre experience from Turkey. *Exp Clin Endocrinol Diabetes* 2009 ; 117 : 345-349.