



Review Article

Challenges and strategies in management of osteoporosis and fragility fracture care during COVID-19 pandemic

Gaurav K. Upadhyaya^a, Karthikeyan Iyengar^b, Vijay K. Jain^{c,*}, Raju Vaishya^d^a Department of Orthopaedics, All India Institute of Medical Sciences, Rae Bareilly, UP, India^b Southport and Ormskirk NHS Trust, Southport, PR8 6PN, UK^c Department of Orthopaedics, Atal Bihari Vajpayee Institute of Medical Sciences, Dr Ram Manohar Lohia Hospital, New Delhi, 110001, India^d Department of Orthopaedics, Indraprastha Apollo Hospital, Sarita Vihar, Mathura Road, 110076, New Delhi, India

ARTICLE INFO

Keywords:

COVID-19
 Coronavirus
 Pandemics
 Osteoporosis
 Fracture
 Spontaneous

ABSTRACT

Background: COVID-19 has resulted in restriction of face to face consultations and mechanisms to access health care. Osteoporosis and fragility fractures forms a significant proportion of adult trauma and orthopaedic workload even during the pandemic.

Aims: We assess the challenges and strategies used in the management of osteoporosis and fragility fracture care during the COVID-19 pandemic.

Methods: We have done a comprehensive review of the literature using suitable keywords on the search engines of PubMed, SCOPUS, Google Scholar and Research Gate in the first week of May 2020 on developments and guidance during the current COVID-19 pandemic.

Results: Osteoporosis and fragility fractures management has been hampered by lock down and infection transmission strategies used to contain the COVID-19 pandemic. Access to diagnostic tests, treatment facilities with the need to use clinical and prediction tools to guide management Telemedicine has an evolving role.

Conclusion: Osteoporosis and fragility fractures in elderly individuals pose a real challenge for an appropriate diagnosis and management, during the COVID-19 pandemic. A clinical decision along with use of clinical prediction tools for osteoporosis should be used to direct treatment. Obligatory fractures such as hip fractures require operative intervention. Non-obligatory fractures such as distal radius fractures can be managed conservatively with use of telemedicine applications in monitoring both types of patients.

1. Introduction

Cornona virus disease (COVID-19) pandemic has had a significant effect on how organizations deliver health care.¹ Trauma and orthopaedic surgery services has been reorganized with significant cancellation of elective surgery to focus on acute clinical priorities on the coronavirus frontlines.² Fragility fractures forms a significant proportion of adult trauma and orthopaedic workload even during the pandemic.³ During the lockdown period the number of injuries due to motor vehicle accidents has come down⁴ but we are still receiving low energy fractures around the hip like neck femur and intertrochanteric fractures, due to osteoporosis. The vertebral fractures due to osteoporosis can lead to chronic pain and deformity with advanced disease. Hip and spine fractures in the elderly are associated with increased mortality, reduction in quality of life, and functional limitations along with substantial economic burden to the health sector which further

compromises the COVID-19 related treatment.⁵ Therapeutic interventions that mitigate fragility fracture in era of COVID-19 are, therefore, essential for reducing the consequences in the future. A patient with osteoporosis requires complete care, multidisciplinary intervention, and patient centric rehabilitation plan; all these will be affected due to COVID-19.⁶

In this comprehensive review we have assessed the impact of challenges posed by COVID -19 in managing osteoporosis and fragility fractures and strategies used to mitigate them.

2. Osteoporosis and India

Osteoporosis is a public health concern all over the world. It is a multifactorial, metabolic bone disease which is characterized by low bone mass, normal mineralization and abnormal bone micro-architecture.⁷ This disruption of bone microarchitecture causes subsequent

* Corresponding author.

E-mail addresses: drgekupadhyaya@yahoo.in (G.K. Upadhyaya), kartikp31@hotmail.com (K. Iyengar), drvijayortho@gmail.com (V.K. Jain), raju.vaishya@gmail.com (R. Vaishya).

<https://doi.org/10.1016/j.jor.2020.06.001>

Received 17 May 2020; Accepted 1 June 2020

Available online 02 June 2020

0972-978X/ © 2020 Professor P K Surendran Memorial Education Foundation. Published by Elsevier B.V. All rights reserved.

and significant increase in the risk for fractures. Osteoporosis affects approximately over 200 million people worldwide. In India, there are around 50 million individuals with osteoporosis or low bone mass.⁸ In India; more than 4.5 million women above the age of 60 years suffered fracture spine and more than 250,000 people sustain a hip fracture every year due to osteoporosis.⁹ Similarly, the total number of fragility fractures in the European Union (EU) is estimated to increase from 2.7 million in 2017 to 3.3 million in 2030; an increase of 23.3%.¹⁰

There are several factors including social and financial reasons which can contribute to osteoporosis in India. These are (i) low intake of Calcium and Vitamin D supplements (ii) unequal distribution of milk and their products, (iii) predominantly vegetarian diet, with phytates and oxalates in fibre-rich Indian food, (iv) avoidance of sunlight exposure, (v) life style change, (vi) lack of physical activity, (vii) Glucocorticoid consumption for different reasons on a long-term, (viii) Genetic differences, (ix) Poor level of awareness and (x) government apathy to bone health.^{11,12} These factors are further affected by lockdown measures, with people staying indoors at home and may be facing poor supply of milk products due to supply and distribution restraints.¹³ With an increase in life expectancy, the percentage of ageing population is increasing and so does the prevalence of osteoporosis and fragility fractures.

Recently there has been emerging and growing evidence that Vitamin D also protect against COVID-19 and to the severity of the disease. The plausible mechanisms include induction of cathelicidins and defensin proteins by vitamin D that can decrease the viral replication rates and COVID-19 related cytokine storm that produce the inflammation in lining of the lungs, leading to pneumonia.¹⁴

3. Fragility fractures

Fragility fractures are fractures that result from mechanical forces that would not ordinarily result in fracture, known as low-level (or 'low-energy') trauma, quantified by The World Health Organization (WHO) as forces equivalent to a fall from a standing height or less. In fact a fragility fracture may be defined as a pathological fracture that results from minimal trauma (e.g. a fall from a standing height) or no identifiable trauma at all.¹⁵ The fragility fracture thus is both a sign and a symptom of osteoporosis. Fragility fractures most commonly affect vertebrae, proximal femur and distal radius; however any bone can be affected by it.¹⁶ There is a likely connection between COVID-19 infection and fragility hip fracture in elderly patients. Fragility fracture can be induced as a result of a fall from a standing due to by fatigue and weakness caused by COVID-19 disease. Therefore COVID-19 infection should be considered in elderly patients with fragility hip fracture during the coronavirus pandemic.¹⁷ Osteoporosis is a major risk factor for fragility fractures.¹⁶ Fragility fractures can be divided into obligatory fractures which require surgery and non-obligatory fractures which can be managed by conservative means.^{18,19}

4. Diagnosis of osteoporosis

The diagnosis of osteoporosis relies on the quantitative assessment of bone mineral density (BMD), usually by central dual energy X-ray absorptiometry (DXA) BMD at the femoral neck provides the reference site. Osteoporosis is defined by the World Health Organization by comparing a patient's bone mineral density (BMD) to that of control at the time of peak bone mass (T-score). Dual energy X-ray absorptiometry (DXA) scan to assess bone mineral density (BMD) is considered as a gold standard for the diagnosis of osteoporosis. It is defined as a value for BMD 2.5 SD or more below the young female adult mean (T-score less than or equal to $-2.5SD$). Severe osteoporosis (established osteoporosis) describes osteoporosis in the presence of 1 or more fragility fractures.

- Normal bone mineral density is within 1 SD

- Low bone mass (osteopenia) is between 1 SD and 2.5 SD below mean peak bone mass
- Osteoporosis is more than 2.5 SD below mean peak bone mass.

5. Challenges and strategies in diagnosis of osteoporosis during COVID-19

However in this situation of COVID-19 pandemic, DEXA scan for BMD assessment is not easily feasible because of the lockdown, travel restrictions and closure of routine services in the hospitals.²⁰ The doctors need to keep a conscious awareness of osteoporosis in their patients and should not stop diagnosing people at risk or those who present with fractures even when they cannot perform full screening tests.²¹

Therefore it increases our dependence on clinical history and osteoporosis related fracture prediction tools. History should be taken to know about any of previous fracture; the Colles' fracture is an early and sensitive indicator of skeletal fragility, predisposing the patient to additional fractures, in particular of the hip.²²

Clinical prediction tools such as Fracture Risk Assessment Tool (FRAX), Osteoporosis self-assessment tool and the Khon Kaen Osteoporosis study score for assessing people at risk for osteoporosis.^{23–25}

Plain radiographs still are helpful and should be taken to recognize osteoporosis. Traditional radiology can possibly diagnose osteoporosis fractures in the most commonly involved sites (spine, pelvis, distal radius, proximal femur and humerus). Vertebral fractures due to bone fragility can be identified easily with vertebral morphometry. The spinal height reduction, make it possible to identify wedge-shaped, biconcave, total vertebral collapse fractures²²

6. Challenges in medical therapy for osteoporosis during the pandemic

Medical management of osteoporosis includes general and pharmacological interventions. **General management** includes assessment of the risk of falls and their prevention. Maintenance of mobility and correction of nutritional deficiencies, particularly of calcium, vitamin D and protein, should be advised. Intakes of at least 1000 mg/day of calcium, 800 IU of vitamin D and of 1 g/kg body weight of protein can be recommended. To reduce the risk of infection, it is recommended that people at risk of COVID-19 should take 10,000 IU/d of vitamin D3 for a few weeks, followed by 5000 IU/d.¹⁴ An adequate intake of calcium rich diet including milk and its derivatives, almonds, cabbage, spinach, turnips and pulses should also be advised. For reduction in fracture risk, particularly in the elderly, the supplementation of calcium should be given who cannot afford nor have availability of these products in their area. Vitamin D is present in animal fats, fish, milk, and dairy products. The patients should be encouraged to consume these products and have walk for at least 30min in their courtyard for proper sun exposure.

Pharmaceutical interventions broadly fall into two categories- Anti restorative drugs and Osteo-anabolic agents. Anti-restorative drugs include Bisphosphonates, Denosumab, Calcitonin, Estrogen and Estrogen receptor modulators. Osteo anabolic agents include Teriparatide and Strontium Ranelate.

The low cost of generic alendronate, which has a broad spectrum of anti-fracture efficacy makes this the first line treatment in the majority of cases.²⁶ In individuals who are intolerant of alendronate or in whom it is contraindicated, other Bisphosphonates, strontium ranelate or raloxifene may provide appropriate treatment options.

However, intravenous use of Zoledronate or Ibandronate in bisphosphonate-naïve or pre-treated patients is associated with acute phase reaction with fever and myalgia. This flu like reaction may occur in up to 50% of patients.^{27,28} The possibility of this flu like reaction which imitate clinical features of COVID-19 infection during the pandemic should be discussed with patients. A laboratory evaluation

should be advised to the patients with impaired renal function and for those at higher risk of developing hypocalcaemia before IV administration of these drugs, which is difficult to arrange in COVID-19 settings. Further these patients require short hospitalization for observation during IV infusion which will be difficult in current scenario when the hospitals are flooded with COVID-19 patients and the transportation is limited in many areas. Additionally, due to the lockdown the demand and supply of these drugs may be affected.²⁰

The patients who are taking parenteral bisphosphonates therefore may be advised for telemedicine consultations with their doctors and to start with oral bisphosphonates without any delay, but with all the precautions; preferably with Alendronate, as it is well studied, and has a good bone binding affinity and safety profile than other oral drugs in this group.²⁶

Patients who are already receiving subcutaneous Denosumab every 6 months may face a difficult choice to continue the treatment without going to healthcare facility. The risk of adverse events of COVID -19 infection increases with use of Denosumab which should be discussed with the patients.²⁹ Furthermore, there may be rapid bone loss within one year of discontinuation of Denosumab and risk of vertebral fragility fractures is increased.^{30–32} Discontinuation of Denosumab should be strongly discouraged by the clinician and patients may be started on oral bisphosphonates. Home visit of health care personnel can be planned for drug administration. Telemedicine services may prove to be helpful in these patients providing video tutorials and education on self-administration of subcutaneous injections of this drug.³³

The high cost of parathyroid hormone peptides restricts their use to those at very high risk, particularly for vertebral fractures. It is also noted that the patients receiving subcutaneous Teriparatide injection treatment can be delayed up to the duration of 3 months.³⁴ If more delay is expected in such patients, then they should be started on oral bisphosphonates on temporary basis till they are able to get a Teriparatide prescription.

With limited evidence, there is concern that COVID-19 infection may be associated with hypercoagulable condition. Estrogen and Selective Estrogen Receptor Modulators such as Raloxifene should be used with caution since these drugs mildly increase the thrombotic risk.^{35,36}

7. Management of fragility fractures

7.1. Obligatory fractures

Fragility hip fractures are usually sustained in the elderly people who have associated co-morbidities. Obligatory fractures such as hip and vertebral fractures with neurological deficit require operative intervention. Patients should be screened and tested for COVID-19 at the emergency setup. All precautions pertaining to COVID-19 should be taken whilst managing patient in the emergency department and on in-patient wards until reports are available. If COVID-19 testing is not possible then a 'Human immunodeficiency virus HIV model', as suggested by Jain V et al.³⁷ can be adopted in the operative management of these patients and every patient should be treated as COVID-19 positive until proved otherwise.³⁷

Confirmed or suspected COVID-19 infection in these patients is not a reason to postpone or cancel hip surgery. British Geriatric Society (BGS) guidelines aim to promote prompt (less than 24 h) consultant-delivered surgical and anaesthetic care where possible.^{18,19} As recommended by the BGS guidelines, a multidisciplinary approach still remains the key in management of these fragility hip fracture patients during the COVID-19 pandemic.¹⁸ It is recommended that elderly patient with hip fractures should undergo minimal invasive procedure which requires less operating time, minimises blood loss, allows immediate post-operative weight-bearing to allow rehabilitation, and reduced length of stay with a primary aim to reduce exposure to coronavirus.^{18,19} Fragility hip fractures can be treated by Cemented bipolar hemi-replacement

arthroplasties or Austin Moore prosthesis for intracapsular fractures and intra or extramedullary implants such as proximal femoral nail or locking dynamic hip screw intertrochanteric fractures. In addition, hemiarthroplasty can enable immediate mobilization and negate the risk of non-union in these cases. Intra-medullary nailing are load bearing and reduces the bone-implant interface. There is a higher mortality rate in patients with a hip fracture in elderly and an associated positive test for COVID-19.³⁸ The patient with hip fractures and COVID-19-positive should be stabilized for respiratory parameters before surgery. The surgery in these cases will provide overall stability of the patient, seated mobilization, improvement in physiological ventilation, and general patient comfort in bed.³⁹ Conservative treatment with traction with immobilization in bed can be considered for high risk COVID-19 patients with comorbidities. However, these bed-ridden patients' should be watched for deep venous thrombosis, urinary tract infections, and hospital-acquired pneumonia.

Absorbable sutures should be used for wound closure wherever possible, to avoid suture removal and a hospital visit.¹⁹ During post-operative period and for rehabilitation, smartphone application and telemedicine facilities can be explored for consultation so that in person visits to the hospital can be avoided.³³

Most osteoporotic vertebral fractures currently have little role for surgical intervention and these patients should be managed conservatively with immobilization using braces. Surgery should be reserved for exceptional cases with presence of neurological compromise.

7.2. Non obligatory fractures

Distal radius fracture, vertebral fracture without neurological deficit or proximal humerus fracture should be managed conservatively, as much as possible. The conservative treatment of an undisplaced vertebral fracture includes analgesic with period of bed rest and walking with a lumbar or thoracic-lumbar support. Fracture of distal radius if displaced should be reduced and maintain in removable splint or plaster of Paris slab. This allows self-removal of splints or plasters at home and avoids an out-patient visit. Similarly most of the fractures of the proximal humerus can be managed with an arm pouch sling. Follow up of these patients can be done through telemedicine facility whenever possible. Other than Plaster of Paris or resin casts, removable splints should be used for fracture management during this COVID-19 pandemic time to decrease the number of visits to healthcare facility. Some degree of mal-union may be accepted and this can be managed by reconstruction surgery in future period, if absolutely necessary.^{40,41}

COVID-19 has made us rethink how we manage fragility fractures. Prioritizing surgical treatment of obligatory fractures in patient care and conservative management of non-obligatory fractures will need ideas for the future including role of telemedicine.

Elimination of modifiable risk factors for osteoporosis (smoking, alcohol abuse) should also be considered during telemedicine.

Immobility is considered a moderate risk factor for osteoporosis. As people are remaining in their homes due to lockdown this is also one of the challenge. Role of the physiotherapy should be properly explained to the patient to prevent fragility fractures. Patients should be prescribed to low or high impact aerobic activity (e.g., indoor walk more than 30 min a day), muscle-strengthening and balance exercises (use of weights for static exercises body exercise bikes).

7.3. Prevention of falls

A fall-prevention strategy for the elderly includes physical exercise, and education regarding risks within the home. The use of hip protector orthosis can be recommended to patients with very high risk of fall.⁴² Use of cane should also be explained to the patients to prevent fall. The factors that can be the source of falls such as physical barriers, wires, rugs, greasy floors, improper footwear, poor lighting and glare from the lamps, etc. must also be corrected.⁴³

8. Future directions

8.1. Role of vaccine

Recently researchers found that bisphosphonates have been used as new vaccine adjuvant eventually helps to shorten the race to COVID-19 immunity.⁴⁴

9. Conclusion

Osteoporosis and the related fractures especially in elderly individuals pose a real challenge for an appropriate management, during the COVID-19 pandemic. Since, the diagnosis of osteoporosis may not be possible by DXA scan; a clinical decision regarding the treatment should be made. Oral vitamin D and Calcium supplementation, along with bisphosphonate therapy, remains the corner stone of treatment of osteoporosis during this crisis, as parenteral therapy may not be feasible. The obligatory fractures like hip and some spinal fractures would require operative intervention, under due precautions of safety from coronavirus infection to the patient and the healthcare workers. To avoid inconvenience of travel, to maintain social distancing and prevent to viral transmission, remote technologies like telemedicine should be employed to supervise the treatment of these patients, as far as possible especially in non-obligatory fracture management.

References

- Nicola M, Alsafi Z, Sohrabi C, et al. The socio-economic implications of the coronavirus and COVID-19 pandemic: a review [published online ahead of print, 2020 apr 16]. *Int J Surg*. 2020;S1743–9191. <https://doi.org/10.1016/j.ijssu.2020.04.018> 20)30316-2.
- Stahel PF. How to risk-stratify elective surgery during the COVID-19 pandemic? *Patient Saf Surg*. 2020;14:8. <https://doi.org/10.1186/s13037-020-00235-9> Published 2020 Mar 31.
- NHS England and NHS Improvement Coronavirus. *Specialty Guides-Major Trauma*. 2020; 2020<https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C0070-specialty-guide-major-trauma-clinical-guide-27-march-2020.pdf>.
- Sahagun L. *Coronavirus Stay-At-Home Orders that Went into Effect on March 20 Have Reduced Vehicle Collisions on California Roadways by Roughly Half*. 01 April 2020<https://www.latimes.com/environment/story/2020-04-01/coronavirus-stay-at-home-orders-have-reduced-traffic-accidents-by-half>.
- Cauley JA. Public health impact of osteoporosis. *J Gerontol A Biol Sci Med Sci*. 2013;68(10):1243–1251. <https://doi.org/10.1093/geronol/glt093>.
- Riemen AH, Hutchison JD. The multidisciplinary management of hip fractures in older patients. *Orthop Trauma*. 2016;30(2):117–122. <https://doi.org/10.1016/j.mporth.2016.03.006>.
- Sözen T, Özişik L, Başaran NÇ. An overview and management of osteoporosis. *Eur J Rheumatol*. 2017;4(1):46–56. <https://doi.org/10.5152/eurjrheum.2016.048>.
- Kaushal N(1, Vohora D(1), Jalali RK(2), Jha S(3). Prevalence of osteoporosis and osteopenia in an apparently healthy Indian population - a cross-sectional retrospective study. *Osteoporosis Sarcopenia*. 2018 Jun;4(2):53–60. <https://doi.org/10.1016/j.afos.2018.04.002> Epub 2018 May 5.
- Mehta N, Garg B, Malhotra R. Management of fragility fractures in India [published correction appears in best pract res clin rheumatol. 2020 feb 24; 101488]. *Best Pract Res Clin Rheumatol*. 2019;33(2):301–309. <https://doi.org/10.1016/j.berh.2019.05.002>.
- Borgström F, Karlsson L, Ortsäter G, et al. Fragility fractures in Europe: burden, management and opportunities. *Arch Osteoporos*. 2020;15(1):59. <https://doi.org/10.1007/s11657-020-0706-y>. Published 2020 Apr 19.
- Mithal A, Bansal B, Kyer CS, EbelingThe P. Asia-Pacific regional audit-epidemiology, costs, and burden of osteoporosis in India 2013: a report of International Osteoporosis Foundation. *Indian J Endocrinol Metab*. 2014;18:449–454.
- Malhotra N, Mithal A. Osteoporosis in Indians. *Indian J Med Res*. 2008;127(3):263–268.
- Haileem A, Javaid M, Vaishya R. Effects of COVID 19 pandemic in daily life [published online ahead of print, 2020 Apr 3]. *Curr Med Res Pract*. 2020. <https://doi.org/10.1016/j.cmrp.2020.03.011> doi:10.1016/j.cmrp.2020.03.011.
- Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*. 2020;12(4):E988. <https://doi.org/10.3390/nu12040988> Published 2020 Apr 2.
- Kanis JA, Oden A, Johnell O, Jonsson B, de Laet C, Dawson A. *Osteoporosis Int*. 2001;12(5):417–427 The burden of osteoporotic fractures: a method for setting intervention thresholds.
- National Institute for Health and Clinical Excellence. *Osteoporosis: Assessing the Risk of Fragility Fracture. NICE Clinical Guideline 146*. London: NICE; 2012 <http://www.nice.org.uk/CG146> accessed on 12 May 2020.
- Shariyate M, Kachooei A. Association of new coronavirus disease with fragility hip and lower limb fractures in elderly patients. *The Archives of Bone and Joint Surgery*. 2020;8:297–301. <https://doi.org/10.22038/abjs.2020.47626.2333>.
- British Geriatrics Society. *Managing Hip Fractures during COVID-19*. 2020; 2020 <https://www.bgs.org.uk/blog/managing-hip-fractures-during-covid19> accessed on 12 May 2020.
- NHS England. 2020; 2020 https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C0086_Specialty-guide-Fragility-Fractures-and-Coronavirus-v1-26-March.pdf accessed on 12 May 2020.
- The Lancet. India under COVID-19 lockdown. *Lancet*. 2020;395(10233):1315. [https://doi.org/10.1016/S0140-6736\(20\)30938-7](https://doi.org/10.1016/S0140-6736(20)30938-7).
- Cimino Steve. *Don't Neglect Osteoporosis Therapy during COVID-19*. May 12,2020; May 12,2020 Say Societies <https://www.medscape.com/viewarticle/930350>.
- Nuti R, Brandi ML, Checchia G, et al. Guidelines for the management of osteoporosis and fragility fractures. *Intern Emerg Med*. 2019 Jan;14(1):85–102. <https://doi.org/10.1007/s11739-018-1874-2>.
- World Health Organization Centre for Metabolic Bone Diseases. FRAX® <http://www.sheffield.ac.uk/FRAX> accessed 12 May 2020.
- Skedros JG(1), Sybrowsky CL, Stoddard GJ. The osteoporosis self-assessment screening tool: a useful tool for the orthopaedic surgeon. *J Bone Joint Surg Am*. 2007;89(4):765–772.
- Pongchaiyakul C, Wanothayaroj E. Performance of the Khon kaen osteoporosis study (KKOS) score for identifying osteoporosis in men. *J Med Assoc Thai*. 2007 Aug;90(8):1518–1523.
- Pazianas M, Cooper C, Ebetino FH, Russell RG. Long-term treatment with bisphosphonates and their safety in postmenopausal osteoporosis. *Therapeut Clin Risk Manag*. 2010 Jul;6:325–343. <https://doi.org/10.2147/tcrm.s8054>.
- Popp AW, Senn R, Curkovic I, et al. Factors associated with acute-phase response of bisphosphonate-naïve or pre-treated women with osteoporosis receiving an intravenous first dose of zoledronate or ibandronate. *Osteoporos Int*. 2017;28(6):1995–2002.
- Crotti C, Watts NB, De Santis M, et al. Acute phase reactions after zoledronic acid infusion: protective role of 25-hydroxyvitamin D and previous Oral bisphosphonate therapy. *Endocr Pract*. 2018;24(5):405–410.
- Diker-Cohen T, Rosenberg D, Avni T, Shepshelovich D, Tsvetov G, Gafter-Gvili A. Risk for infections during treatment with denosumab for osteoporosis: a systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2020 May 1(5):105. <https://doi.org/10.1210/clinem/dgz322> pii: dgz322.
- Miller PD, Wagman RB, Peacock M, et al. Effect of Denosumab on bone mineral density and biochemical markers of bone turnover: six-year results of a phase 2 clinical trial. *J Clin Endocrinol Metab*. 2011;96(2):394–402.
- Bone HG, Bolognese MA, Yuen CK, et al. Effects of denosumab treatment and discontinuation on bone mineral density and bone turnover markers in postmenopausal women with low bone mass. *J Clin Endocrinol Metab*. 2011;96(4):972–980.
- Cummings SR, Ferrari S, Eastell R, et al. Vertebral fractures after discontinuation of denosumab: a post hoc analysis of the randomized placebo-controlled FREEDOM Trial and its extension. *J Bone Miner Res*. 2018;33(2):190–198.
- Greenhalgh T, Wherton J, Shaw S, Morrison C. Video consultations for covid-19. *BMJ*. 2020;368:m998. <https://doi.org/10.1136/bmj.m998> Published 2020 Mar 12.
- Joint Guidance on Osteoporosis Management in the Era of COVID-19 from the American Society for Bone and Mineral Research (ASBMR), American Association of Clinical Endocrinologists (AAACE), Endocrine Society, European Calcified Tissue Society (ECTS) and National Osteoporosis Foundation (NOF).
- Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Haematological findings and complications of COVID-19. *Am J Hematol*. 2020 Apr 13. <https://doi.org/10.1002/ajh.25829> [Epub ahead of print].
- Spiezia L, Boscolo A, Poletto F, Cerruti L, Tiberio I, Campello E. COVID-19 related severe hypercoagulability in patients admitted to intensive care unit for acute respiratory failure. *Thromb Haemostasis*. 2020 Apr 21. <https://doi.org/10.1055/s-0040-1710018> [Epub ahead of print].
- Jain VK, Vaishya R. COVID-19 and orthopaedic surgeons: the Indian scenario. *Trop Doct*. 2020;50(2):108–110. <https://doi.org/10.1177/0049475520921616>.
- Muñoz Vives JM, Jornet-Gibert M, Cámara-Cabrera J, et al. Mortality rates of patients with proximal femoral fracture in a worldwide pandemic: preliminary results of the Spanish HIP-COVID observational study. *J Bone Joint Surg Am*. 2020 May 6, 127(3). doi: 10.2106/JBJS.20.00686. Online ahead of print.
- Catellani F, Coscione A, D'Ambrosi R, Usai L, Roscitano C, Fiorentino G. Treatment of proximal femoral fragility fractures in patients with COVID-19 during the SARS-CoV-2 outbreak in northern Italy [published online ahead of print, 2020 apr 28]. *J Bone Joint Surg Am*. 2020. <https://doi.org/10.2106/JBJS.20.00617> doi:10.2106/JBJS.20.00617.
- NHS England and NHS Improvement Coronavirus. *Specialty Guides-Major Trauma*. 2020; 2020<https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C0070-specialty-guide-major-trauma-clinical-guide-27-march-2020.pdf>.
- British Orthopaedic Association. *Specialty Guidelines*. 2020; 2020 <https://www.boa.ac.uk/uploads/assets/ee39d8a8-9457-4533-9774e973c835246d/COVID-19-BOASTs-Combined-v1FINAL.pdf> accessed 12May 2020.
- Kannus P, Parkkari J. Prevention of hip fracture with hip protectors. *Age Ageing*. 2006 Sep;35 Suppl 2:ii51–ii54. Review.
- Vaishya R - Vaish A. Falls in older adults are serious. *Indian J Orthop*. 2020;54:69–74.
- Faster Protection with Less Material. <https://news.harvard.edu/gazette/story/series/coronavirus/> Accessed 12 May 2020.