Endocrine (2012) 41:347–349
DOI 10.1007/s12020-012-9640-0

EDITORIAL

An increased risk for fractures: another cause of frailty in HIV-infected subjects

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Published online: 8 March 2012

Antiretroviral therapy (ART) has determined a huge decline in morbidity and mortality directly due to AIDS in HIV-infected subjects [1]. Nevertheless, a significant increase in the occurrence of several clinical conditions, such athero-thrombotic pathologies (coronary artery disease, stroke, peripheral artery disease) [2], lung [3] and liver diseases [4], cancers not related to AIDS (especially hepatocellular carcinoma, Hodgkin's lymphoma and lung cancer) [5] have been observed. In addition, a high prevalence of several cardio-metabolic risk factors, such as insulin resistance, lipodystrophy, hyperglycemia [1], hypertension [6], hyperlipidemia [1], metabolic syndrome [1, 7, 8] have been documented. All these clinical and metabolic conditions seem to be at least partially due to a direct action of HIV but over all to ART. In addition, HIV-infected people could have a premature aging due not only to multiple co-morbidities but also to other potential causes, such as immune-aging possibly related to persistent immune activation, behavioral risk factors (smoking, excessive alcohol intake, unhealthy diet), adverse effects of ART [9]. Therefore, HIV-infected subjects can have several causes of frailty; this implies that their quality of life and life expectancy, although improved in the era of ART, are worse than those of non-HIV subjects. Torti and colleagues have recently shown that HIV-infected males can have a significant increase in the risk for vertebral fractures [10]. The prevalence of fractures was significantly greater in HIV-patients than in age-comparable controls, and interestingly the fracture rate was greater in patients on ART than in drug-naïve subjects [10]. All subjects with known potential causes of osteoporosis, including menopause, were excluded from the study; indeed to avoid the interference of menopause only men were recruited. The results of the study clearly suggest that the increased risk for fractures seems to be mainly due to HIV-infection and its treatment [10, 11]. Several previous studies had shown that bone mineral mass is decreased in a large proportion of the HIV-infected population and therefore it was suggested that subjects living with HIV could be more prone to fractures than non-infected subjects [12]. Nevertheless, until now a few data were available in the literature on this topic. The paper by Torti has the merit to document that really there is an increased prevalence of fragility fractures among HIV-infected patients [10]. Obviously other work has to confirm this finding and in particular longitudinal data are needed. However, the study by Torti suggest some important considerations. The increased risk of fractures can greatly worsen the condition of frailty due to clinical conditions associated to HIV-infection and its treatment. On the other hand a dangerous interplay between these conditions is possible. Torti and colleagues have hypothesized that insulin resistance and diabetes can contribute to the high risk for fractures in HIV-infected patients [10]. Really it is well-known that insulin resistance can affect bone metabolism [13] and diabetes can have an independent role in the occurrence of fractures also in other conditions [14]. Taken together, all these data suggest that the increased risk for fractures should be early considered together with all other clinical conditions in HIV-infected

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subjects. Indeed, all these conditions can occur quite early and often involve many organs and systems. Therefore, the prevention, assessment, and early treatment of every hypothetical abnormality should be started as soon as possible. In other words, the effective management of the HIV-infection has to be addressed not only to the control of viral replication but also to every associated condition. In this perspective, the role of the general practitioner and the specialist in infectious diseases is crucial. In particular, they can prevent, detect and early treat any possible abnormality associated to HIV-infection. In several patients it is possible to avoid or treat some conditions simply by varying the combinations of ARTs. When associated conditions require more complex checks and therapies, a multidisciplinary approach is mandatory through referral the patients to other specialists, such as endocrinologist, diabetologist, cardiologist, internist, and rheumatologist. To prevent or minimize the impact of HIV-infection and ART on the bone, it is important to increase calcium intake (from milk and derivates), sun exposure, and physical activity, to reduce coffee, salt, and alcohol intake, and to early initiate calcium and vitamin supplementation. A specific pharmacologic treatment should be taken into account on the basis of a DXA scan [15, 16]. But it is unclear when DXA scan should be performed. Indeed, in the study by Torti vertebral fractures occurred in most patients without indications to perform DXA scan on the basis of the FRAX algorithm [17]. Current guidelines on the osteoporosis do not take into account HIV-infection among risk factors that require a screening for osteoporosis in younger subjects [18, 19]. HIV should be added to the list of risk factors for osteoporosis and probably a DXA should be performed in all HIV-infected patients 50 years or older, as recently suggested [12]. However, in HIV-infected patients bone mass density, as assessed by DXA scan, may underestimate the risk for fractures, as also seen in other types of secondary osteoporosis [14]; therefore it may be useful to perform not only DXA scan but also a spine radiography [14]. In addition, some authors have recently suggested to use some turnover markers as a complement to DXA scan, in order to better and early identify bone integrity/damage in HIV-infected individuals [20].

In conclusion, increased risk for fragility fractures may represent another important cause of frailty that adds itself to those involving several organs and systems and that can reduce quality of life and life expectancy in HIV-infected subjects. Any effort should be made to prevent all conditions associated with HIV-infection, including the risk for fractures, by a systematic multidisciplinary approach.

Conflict of interest None.

References

1. A.D. Gutierrez, A. Balasubramanyam, Dysregulation of glucose metabolism in HIV patients: epidemiology, mechanisms, and management. Endocrine **41**, 1–10 (2012)
2. F. Fedele, N. Bruno, M. Mancone, Cardiovascular risk factors and HIV disease. AIDS Rev. **13**, 119–129 (2011)
3. A. Morris, M.P. George, K. Crothers, L. Huang, L. Lucht, C. Kessinger, E.C. Kleerup, HIV and chronic obstructive pulmonary disease: it is worse and why? Proc. Am. Thorac. Soc. **8**, 320–325 (2011)
4. O. Falade-Nwulia, C.L. Thio, Liver disease, HIV and aging. Sex. Health **8**, 512–520 (2011)
5. K. Sigel, R. Dubrov, M. Silvergerg, K. Crothers, S. Braithwaite, A. Justice, Cancer screening in patients infected with HIV. Curr. HIV/AIDS Rep. **8**, 142–152 (2011)
6. C. Gazzaruso, R. Bruno, A. Garzaniti, S. Giordanetti, P. Fratino, P. Sacchi, G. Filice, Hypertension among HIV-patients: prevalence and relationships to insulin-resistance and metabolic syndrome. J. Hypertens. **21**, 1377–1382 (2003)
7. C. Gazzaruso, P. Sacchi, A. Garzaniti, P. Fratino, R. Bruno, G. Filice, Prevalence of metabolic syndrome among HIV patients. Diabetes Care **25**, 1253–1254 (2002)
8. R. Bruno, C. Gazzaruso, P. Sacchi, C. Zocchetti, S. Giordanetti, A. Garzaniti, V. Ciappina, E. Maffezzini, R. Maserati, G. Filice, High prevalence of metabolic syndrome among HIV-infected patients: link with the cardiovascular risk. J. Acquir. Immune Defic. Syndr. **31**, 363–365 (2002)
9. B. Hasse, B. Ledergerber, H. Furrer, Swiss HIV Cohort Study. Morbidity and aging in HIV-infected persons: the Swiss HIV cohort study. Clin. Infect. Dis. **53**, 1130–1139 (2011)
10. C. Torti, G. Mazziotti, P.A. Soldini, E. Focà, R. Maroldi, D. Gotti, G. Carosi, A. Giustina, High prevalence of radiological vertebral fractures in HIV-infected males. Endocrine. (2011). doi: 10.1007/s12020-011-9586-7
11. G. Mazziotti, E. Canalis, A. Giustina, Drug-induced osteoporosis: mechanisms and clinical implications. Am. J. Med. **123**, 877–884 (2010)
12. G.A. McComsey, P. Tebas, E. Shane et al., Bone disease in HIV infection: a practical review and recommendations for HIV Care Providers. Clin. Infect. Dis. **51**, 937–946 (2010)
13. R.M. Campos, A. de Piano, P.L. da Silva, et al., The role of pro/anti-inflammatory adipokines on bone metabolism in NAFLD obese adolescents: effects of long-term interdisciplinary therapy. Endocrine. (2012). doi:10.1007/s12020-012-9613-3
14. G. Mazziotti, M. Gola, A. Bianchi et al., Influence of diabetes mellitus on vertebral fractures in men with acromegaly. Endocrine **40**, 102–108 (2011)
15. G. Mazziotti, J. Bilezikian, E. Canalis, D. Cocchi, A. Giustina, New understanding and treatments for osteoporosis. Endocrine **41**, 58–69 (2012)
16. J. Compston, The use of combination therapy in the treatment of postmenopausal osteoporosis. Endocrine **41**, 11–18 (2012)
17. J.A. Kanis, E.V. McCloskey, H. Johansson, O. Strom, F. Borgstrom, National Osteoporosis Guideline Group. Case finding for the management of osteoporosis with FRAX–assessment and intervention thresholds for the UK. Osteoporosis Int. **19**, 1395–1408 (2008)
18. N.O. Foundation, *Clinician's guide to prevention and treatment of osteoporosis* (National Osteoporosis Foundation, Washington, 2010)

19. S. Adami, F. Bertoldo, M.L. Brandi et al., Guidelines for the diagnosis, prevention and treatment of osteoporosis. Reumatismo **61**, 1–25 (2009)
20. E. Focà, D. Motta, M. Borderi et al., Prospective evaluation of bone markers, paratormone and 1,25-(OH)2 vitamin D in HIV-positive patients after the initiation of tenofovir/emtricitabine with atazanavir/ritonavir or efavirenz. BMC Infect. Dis. **12**, 38 (2012)