BAISHIDENG PUBLISHING GROUPINC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

RESPONSES TO REVIEWER`S COMMENTS

Query 1. Given that the use of quantification of MP as a clinical tool is still controversial, the comparisons between different methods to measure MP should be discussed.

Answer: We added following two paragraph to article to address this query

"*Although there is consensus on the importance of EMPs, obtained results may show variation even within the same disease likely due to diversity in methodology used for microparticle measurement* [34]. *For example, freezing may decrease EMPs level regardless of storage duration* [34]. *In another study* [35], *It was demonstrated that there was no significant difference in terms of the levels of EMPs between fresh and frozen samples, however, long term storage of samples at -80°, all types of MPs were significantly reduced.*

Solid phase capture assay, flow cytometry and ELISA have been used to identify and measure EMPs level in blood. The solid-phase capture assay is able to perform the capture of most of MPs and functional assessment of the circulating MPs having procoagulant potential, irrespective of the capture ligand. The most important weakness of this method is underestimation of MP levels by antigenic capture due to possible interaction of soluble antigens [36]. *Flow cytomety is the most widely used technique to quantify EMPs. It can capable of the analysis of thousands of MPs and differentiate the MPs based on their cellular origins* [35,36]. *Major disadvantages of flow cytometry are its labor-intensiveness, costs and ineffective to detect MPs smaller than 300 nm in diameter* [34-36]. "

Query 2. To serve as a marker, measurement of MP for age- or gender-related heterogeneity needs normalization. What is the normal reference of MP in adult and pediatric population? Any gender difference? Is its level related to CKD staging?

Answer: We tried to give more detail about this query. Unfortunately, we could add only two sentences based on the current literature about this topic. It is following sentence:

"Unfortunately, we do not have data giving the normal reference of MP in adult and pediatric population and its level based on CKD stage. Recently, we have demonstrated the patients with CKD stage 3-5 had increased EMPs compare to control subjects [11]."

Query 3. Can endothelial MP serve as a marker for therapeutic response? Any reports about specific MP-lowering medication?

BAISHIDENG PUBLISHING GROUPINC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

Answer

"Some interventions such as fish-oil supplementation, statins, anti-TNF agents, acetylsalicylate and vitamin C supplementation may affect microparticle formation and reduce number of circulating microparticles [18-22]. For this reason, analysis of circulating microparticles could give useful information about the efficacy of treatment [23]."

Query 4. Although the authors showed the relationships between MP and arterial stiffness (e.g., PWV), what is its role on hypertension and CV mortality in patient with CKD?

Answer

"Although the reason of the increased circulating EMPs in hypertensive patients is not completely clear [40], it has been shown that EMPs may induce the progression of impaired endothelial function that already exists via expression of different adhesion molecules, endothelial cyclooxygenase type 2, the release of cytokines, and the impairment of nitric oxide released from vascular endothelial cells [23,25]. This may cause atherosclerosis, hypertension and target organ damage such as hypertensive nephropathy, which is one of the common complications of high blood pressure. Hypertension is one of the leading causes of CKD in adult and EMPs are involved in impaired renal function in patients with hypertension [41]. Hsu et al [41] studied the relationship between circulating MPs and decline in GFR in hypertensive subjects and demonstrated that the ratio of circulating EMP to endothelial progenitor cell (EPC) was associated with deterioration of kidney function. This is likely explained by the impaired vascular repair capacity and increased endothelial damage indicated by higher EMP to EPC ratios may accelerate the decline in GFR in patients with hypertension [41]."

Query 5. The authors might provide the major blocks for future clinical application of MP.

Minor points: 1.

There is lack of page number. I have put it already

2. There are some typos, such as "glomerulonephritides" and "micropartciles".

We changed them according to your advise