1. Response to **Reviewer** 02860897

   Thanks for the advice and suggestion for this manuscript.

   (1) Response to major 1. What is the major determinant for cTAC. Is it a protocol of TAC or genetic background of patients?

   Firstly, for most recipients, the adjustment of cTAC is according to a protocol described in the method. Our center adopted the standard tacrolimus regimen with 0.05-0.10 mg/kg per day at the early stage after liver transplantation, especially during the first 3 moths, to maintain the cTAC within the range of 5-10 ng/mL.

   Secondly, after 6 months, the tacrolimus strategy is individually adjusted depending on allograft function. We began to tailor the tacrolimus dosage to decrease the cTAC as low as possible without rejection episode.

   Thirdly, recipients achieved different cTAC maintenance level during the follow-up periods after 6 months. Previous studies have reported that there are certain genes expression in the clinical operational tolerant recipients. There is no recipient achieving in discontinuing the immunosuppressants in our center, so we adopt the minimum tacrolimus strategy. A pilot study about the gene expression profile in the recipients with successful low tacrolimus exposure (i.e. almost clinical tolerance status) is performed in our center. So we believe that, we may choose the certain recipients to reduce the cTAC safely and effectively in next step.

   (2) Response to major 2. Clarify the role of confounding factors that affect insulin resistance and reduction of insulin secretion.

   Firstly, a recent meta-analysis (Sharif A, Shabir S, Chand S, Cockwell P, Ball S, Borrows R. Meta-analysis of calcineurin-inhibitor-sparing regimens in kidney transplantation. J Am Soc Nephrol 2011; 22:2107-2118.) of 56 randomized controlled trials demonstrated less PTDM and better overall graft survival with reduced CNI exposure. So we hypothesized that high cTAC may be an independent risk factor for NODM.

   Secondly, several factors are significant in the univariable analysis. However, only the age (>50), pre-LT hypertension and high cTAC (≥ 5.89) are independent risk factor in multivariable regression analysis.

   (3) Response to minor.

   The language of this manuscript has been revises by native English speaker.

2. Response to **Reviewer** 02446566

   Thanks for the advice and suggestion for this manuscript.

   (1) Response to the question of "whether the threshold of trough of tacrolimus is different if the patients are classified according to the age or pre-transplantation hypertension". we reanalyzed the data and found that the cutoff value of tacrolimus concentration is 5.99 in older recipients (age＞50, n=139), and is 5.86 in younger recipients (age ≤50, n=389). As the difference is not too obvious, so we think the recipient age did not influence the cutoff value of 5.89 significantly. Additionally, there are only 12 recipients (2.3%) diagnosed as hypertension before liver transplantation, and we think that this factor is not necessary to consider.

   (2) Response to the minor mistyping. We have corrected the mistyping mentioned in the highlighted section.

3. Response to **Reviewer** 02446585

   Thanks for the advice and suggestion for this manuscript.

   (1) The language of this manuscript has been revises by native English speaker.

   (2) We have omitted the non-relevant data, including *blood type (O/A/B/AB)*, *autoimmune hepatitis* and *new-onset malignance post-LT* in table 1; and omitted the data of *blood type (O/A/B/AB)* and *autoimmune hepatitis* in table 3. All the remove contents are highlighted in reversion manuscript.