Birth Weight and Renal Functional Reserve in Adults

To the Editor: We read with great interest the paper "Renal Functional Response-Association With Birth Weight and Kidney Volume" by Lillås *et al*.[1] Low birth weight (LBW) is a well-known surrogate marker for nephron endowment and is associated with impaired salt handling and glomerular hyperfiltration, leading to the development of hypertension and progression to end-stage kidney disease in later life.[2,3] Because the number of nephrons in humans does not increase after term birth, individuals with a low nephron number are thought to have limited adaptive capacity to maintain normal renal function under various stress conditions. Lillås *et al*.[1] examined the possibility of reduced renal functional response (RFR) in adult subjects born with LBW. RFR refers to the increase in total glomerular filtration rate induced by an acute dietary protein load and has been used to quantitatively assess the adaptive reserve function of the kidneys.[4] The results of this study showed that RFR was positively correlated with kidney volume and more strongly inversely correlated with glomerular filtration rate per kidney volume, but not with LBW. The greatest strength of this study is the demonstration that RFR can be quantified as a more convenient measure derived from a combined assessment of glomerular filtration rate and kidney volume. Nevertheless, the results of this study may not be sufficient to conclude that LBW is not associated with lower RFR. In this study, mean gestational age of the LBW group was 34 weeks for men and 35 weeks for women. Therefore, most LBW subjects were born in the "near term" of gestation. Because human nephron number is determined by 32 to 36 weeks,[5] the number of nephrons in the LBW group in this study may not have been low enough to affect RFR in adulthood. As the authors mention, it should also be noted that a significant number of the candidate subjects in this study whose RFR may have been reduced because they actually had considerably fewer nephrons may have been excluded because of hypertension or other health concerns.

1. Lillås BS, Tøndel C, Melsom T, Eriksen BO, Marti H-P, Vikse B. Renal functional response-association with birth weight and kidney volume. *Kidney Int Rep*. 2023;8:1034–1042. https://doi.org/10.1016/j.ekir.2023.02.1079
2. Brenner BM, Garcia DL, Anderson S. Glomeruli and blood pressure. Less of one, more the other? *Am J Hypertens*. 1988;1:335–347. https://doi.org/10.1093/ajh/1.4.335
3. Luyckx VA, Bertram JF, Brenner BM, et al. Effect of fetal and child health on kidney development and long-term risk of hypertension and kidney disease. *Lancet*. 2013;382:273–283. https://doi.org/10.1016/S0140-6736(13)60311-6
4. Bosch JP, Saccaggi A, Lauer A, Ronco C, Belledonne M, Glabman S. Renal functional reserve in humans. Effect of protein intake on glomerular filtration rate. *Am J Med*. 1983;75:943–950. https://doi.org/10.1016/0002-9343(83)90873-2
5. Hinchliffe SA, Sargent PH, Howard CV, Chan YF, van Velzen D. Human intrauterine renal growth expressed in absolute number of glomeruli assessed by the disector method and Cavalieri principle. *Lab Investig*. 1991;64:777–784.

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Response to Birth Weight and Renal Functional Reserve in Adults

The author Replies: In this issue Tsuboi and Bertram[1] have commented on our paper "Renal functional response–association with birth weight and kidney volume."[S1] We would like to thank the authors for their appreciation of our research and for questioning the level of prematurity of our low birth weight (LBW) cohort. It is argued that being born close to term, yet premature, the kidneys of the LBW group may have been too well developed to allow for a reduced renal functional response. This is a valid argument that unfortunately was not discussed in our paper. However, we did not find any association between gestational age