Complex haemodynamic study of the renal artery and its vascular environment

PhD theses

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1. Introduction

1.1. Flow and physiological implications of renal artery vascular geometry

The geometry of the renal artery and its surroundings has been investigated in several aspects in previous studies. The difference between the branching angles of the right and left renal arteries has been discovered [1]. The peculiar angle of the branching and the difference between the two sides can be of great importance.

The effect of renal artery hemodynamics may be even greater in patients with renal disease with solitary kidney. It is hypothesized that the hemodynamic state of the renal artery is more sensitive to changes in blood pressure in this state.

The angle of arterial branching in native kidneys is different from that in transplanted kidneys. This may affect the hemodynamic state and indirectly the function of the transplanted kidney. There are currently no data suggesting that renal artery branching angle is taken into account in the practice of kidney transplantation.

1.2. The finite element numerical flow simulation

The finite element method (FEM) is a computational technique for solving differential equations describing the behaviour of a system [2]. The basic principle of the finite element method is that a large, complex system is divided into smaller, simpler parts (elements) that can be examined individually and then reassembled to obtain the solution for the whole system.

2. Objectives

1. Is the average eGFR after transplantation of donor kidneys transplanted on the same side different from that of donor kidneys transplanted on the opposite side?
2. Does the average native renal artery branching angle differ between the right and left side?
3. Does the renal artery branching angle affect the haemodynamic parameters of the native two-kidney and single-kidney condition or the transplanted kidney?
4. Is there an optimal range for the renal artery branching angle?
5. How does hypertension affect renal artery haemodynamics, how does it change in the case of solitary kidney?
6. Is isolated systolic hypertension also likely to affect renal artery haemodynamics, and to what extent in the case of solitary kidney?

3. Methods

The data were collected and used in accordance with the ethical approval No. 7504-PTE 2018 issued by the Regional Research Ethics Committee of the University of Pécs. The data were handled in accordance with the provisions of Acts LXIII of 1992 and XLVII of 1997; and with the provisions of Annex 3 ("Code of Ethics for Scientific Research") of the Research, Development and Innovation Strategy of the University of Pécs.

Two retrospective clinical studies and numerical flow simulations were performed:

Study 1:

In a longitudinal study, we investigated the early adaptation of transplanted kidneys during the first ten days after transplantation.

Study 2:

In the second study, we measured the right and left branching angles of the aorta and the renal artery of a randomly selected group of patients in vivo and performed measurements to determine the idealized geometry model for the finite element analysis.

Study 3:

a. A series of numerical flow simulations were performed to determine the hemodynamic effects of the renal artery branching angle in healthy and single-kidney cases.

b. Numerical flow simulations were performed to investigate the effects of hypertension and isolated systolic hypertension on renal artery hemodynamics in healthy and single-kidney cases.

3.1. Study 1: measurement of eGFR in kidney transplant recipients after kidney transplantation

Differences in estimated glomerular filtration rate (eGFR) values after transplantation were investigated in 46 randomly selected patients. Two groups were compared in this respect, one group included those who received a right donor kidney for the right side (n1=20), the other group was those who received a left donor kidney for the right side (n2=26).

Of the 172 patients initially identified, 116 had no recorded data on the donor kidney side. Of the remaining patients, the transplantation to the right side was performed in 46 patients and to the left side in only 10 patients, and the latter were excluded from the analysis due to statistically insufficient data.

3.2. Study 2: measurement of the renal artery branching angle

In our retrospective study, we measured in vivo the branching angle of the renal artery of the aorta on the right and left side in a randomly selected group of patients and performed measurements to determine the geometry of the idealised finite element model. Angle measurements were performed in 44 randomly selected patients (mean age 60 years, 29 women, 15 men, minimum age 38 years, maximum age 76 years) on existing catheter-based biplane X-ray angiography images. The scans were provided in video format by the Department of Cardiology, Clinical Centre, University of Pécs.

3.3. Test 3: numerical flow simulation

To determine the hemodynamic effects of the branching angle and blood pressure on the renal artery, a series of numerical flow simulations were performed to measure the area weighted average total pressure, turbulent kinetic energy, velocity and volumetric flow in the right and left renal arteries.

It has been shown, and the literature suggests, that real geometric models constructed from images obtained during imaging procedures still have many confounding morphological differences that may distort the results [1]. Therefore, an idealized model is needed to separately investigate the effects of the branching angle, unbiased by any other geometric factors.

The input boundary condition applied on the aortic cross-section was a transient velocity waveform characteristic of the aorta, varying over a cardiac cycle [3]. The boundary condition applied on the arterial wall was a no-slip boundary condition.

The viscosity model used in the simulation is the widely used "realizable k-ε viscosity model" [4]. In order to obtain a model that well describes the behavior of the fluid flow layers near the wall, an appropriate computational method had to be chosen. The Menter-Lechner [5] near-wall calculation method with curvature correction [6] was used.

3.3.1. 3/a. Study: a series of simulations to study the effect of the renal artery branching angle

To explore the effect of the renal artery branching angle on the flow parameters, a series of simulations were performed as described previously.

For these simulations, a series of models were created where the right renal artery branching angle was kept constant with an average angle of 66°, while the left renal artery branching angle was varied between the minimum (49°) and maximum (138°) measured value in 10 degree increments. The angles analysed in the simulation are summarised in Table 1.

Table 1. Angles analyzed in the simulation

Number of simulation	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
Left renal artery branching angle	49°	59°	69°	79°	89°	99°	109°	119°	129°	138°
Right renal artery branching angle	66°	66°	66°	66°	66°	66°	66°	66°	66°	66°

Single kidney models were also created and used in the simulations to compare them with previous results and to determine the effect of the presence of the right renal artery on the hemodynamic characteristics of the left renal artery.

3.3.2. Study 3/b: a series of simulations to study the effects of blood pressure

A new series of simulations was performed to investigate the effects of changes in blood pressure on the flow characteristics of the renal artery. The aim of the study was to investigate the differences between the single kidney and the healthy state. In both the single kidney and healthy models, 12 blood pressure values were included as shown in Table 2, for a total of 24 simulations.

Table 2. Blood pressure values used in the simulation (Hgmm)

Analysis	Hypertension disease								Isolated systolic hypertension			
Sys.	120	140	150	160	170	180	190	200	200	200	200	200
Dia.	80	90	90	90	90	90	90	90	80	70	60	50

To simulate hypertension, we initially increased both systolic and diastolic blood pressure values up to 200/90 mm Hg. For further studies, we simulated isolated systolic hypertension by reducing diastolic blood pressure from 200/90 mm Hg to 200/50 mm Hg, while maintaining systolic blood pressure

4. Results

4.1. Study 1: measurement of eGFR in kidney transplant recipients after kidney transplantation

Figure 1 shows the change of eGFR values of the two groups as a function of time in the first 10 days after transplantation. Values with a significant difference in eGFR are marked with stars. In the analysis of post-transplant eGFR values, we found that patients who had a right donor kidney transplanted to the right side had a significantly higher mean eGFR value by the third day after transplantation than patients who had a left donor kidney transplanted to the right side. The eGFR values of both groups increased over time, but the difference between the values remained consistent.

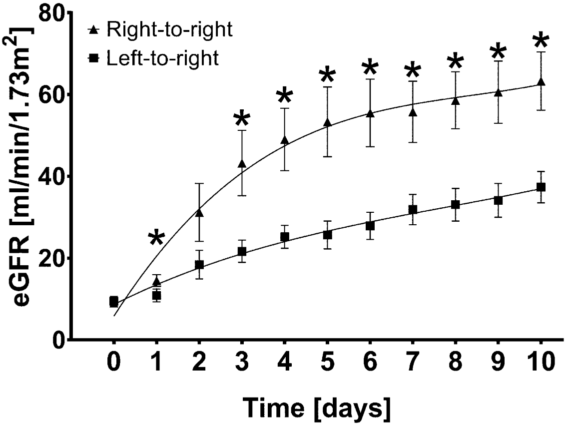

Figure 1. eGFR values of right-right and left-right kidney transplant patient groups as a function of time.

4.2. Study 2: measurement of the renal artery branching angle

The average angle was 66° on the right side and 78° on the left. The difference between the angles of the two sides was found to be significant (P=0.001).

4.3. 3/a. Study: a series of simulations to study the effect of the renal artery branching angle

The results obtained from the simulations show a clear difference between the hemodynamic state of the left and right renal arteries, as shown in Figure 2. The figure shows the turbulent kinetic energy values in the left and right renal arteries during one cardiac cycle, starting at the beginning of the systolic phase. The figure also shows the geometry of the model, with average renal artery branching angles on both sides.

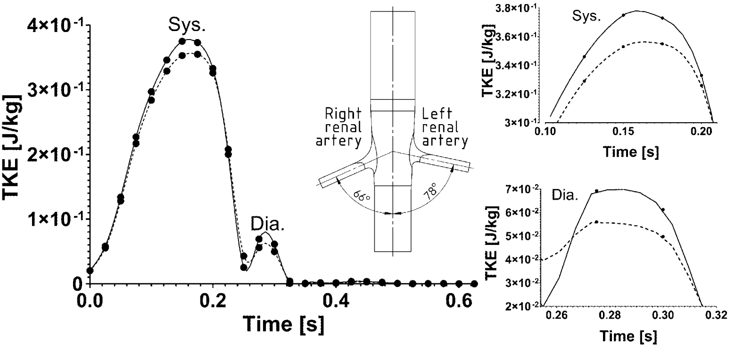

Figure 2. Area-weighted average turbulent kinetic energy (TKE) as a function of time in the renal arteries during one cardiac cycle in an idealized model with statistically average branching angle on both sides, calculated by computational fluid dynamics simulation.

The results of the simulations showed a considerable difference between the haemodynamic status of the left and right renal arteries. TKE on the left side showed a higher maximum in both systolic and diastolic phases.

A pressure difference was observed between models with maximum, mean and minimum left renal artery branching angles. The TKE values showed even more pronounced differences than the pressure values for the maximum, average and minimum left renal artery branch angle models. The pressure drop is the largest in a model with the maximum left bifurcation angle, supporting previous findings.

It is important to note that the minimum volumetric flow is negative in all models, implying that backflow is present during the cardiac cycle.

A series of simulation models was created by gradually increasing the branching angle of the left renal artery in 10° increments. The simulations carried out on these showed that there could be an optimal renal artery branching angle range between 58° and 88°, within which the output flow parameters (pressure, velocity, volume flow) were relatively constant, and higher outside this range. On the other hand, the nature of the turbulent kinetic energy, which may influence the risk of atherosclerotic lesions in renal arteries, was different from the other parameters. The optimal range of turbulent kinetic energy was between 58-78°, outside this range values were higher.

4.4. Study 3/b: a series of simulations to study the effects of blood pressure

The results of the series of simulations performed to study hypertension show that increasing systolic blood pressure increases the difference between the systolic values of the haemodynamic variables of the single kidney and healthy states. The difference between the diastolic values does not change.

For high systolic with reduced diastolic blood pressure, there is no marked change in systolic values, and diastolic output pressure is reduced as expected in both models. This difference occurs at a smaller change in the solitary kidney case than in the healthy model. The diastolic values of velocity, volumetric flow and turbulent kinetic energy increased as expected with a decrease in aortic diastolic blood pressure in both models. There was no difference in the change between the two models.

5. Discussion

5.1. Main findings of the research

The findings of the research are:

1. patients who had a right donor kidney transplanted to the right side had a significantly higher mean eGFR after transplantation than patients who had a left donor kidney transplanted to the right side.

2. The mean native renal artery branching angle is 66° on the rights side and 78° on the left side.

3. The renal artery branching angle influences the hemodynamic parameters of the healthy and single kidney states.

4. The optimal range of renal artery branching angle is 58-78° on the left side.

5. High blood pressure alters the flow characteristics of the renal artery, to a greater extent in the case of solitary kidney.

6. Isolated systolic hypertension also affects the flow characteristics of the renal artery, to a greater extent in the case of solitary kidney.

5.2. Relationship between branching angles and eGFR after kidney transplantation

The adaptation of the transplanted kidney after transplantation is characterized by the recovery of renal function. In our present analysis (study 1), a clear separation of graft function was observed between the two groups studied (Figure 1.). It is important to note that the observed eGFR changes after transplantation are due to hemodynamic differences. We hypothesized that the difference in renal artery branching angle between the two sides may play a role in this phenomenon, a possibility that has not been previously considered. Our results suggest that renal artery branching angle may play a role in early adaptation after kidney transplantation.

5.3. Consequences of the state of solitary kidney

Our results show that the single kidney condition can also result in hemodynamic changes. We measured higher pressures and TKE at the outlet cross-section of the renal artery in the single kidney models than in the healthy models. This effect may be even stronger at higher renal artery branching angles. The effect of high blood pressure also results in a greater change in the pressure and turbulent kinetic energy values measured in the renal artery of the single kidney models than in the healthy models.

5.4. The optimal renal artery branching angle

The optimal renal artery branching angle ranges are shown in Figure 3. It demonstrates the changes in flow characteristics and their consequences in the suboptimal range. The figure shows the silhouette of the idealized aorta-renal artery branching model in white with average angle values on both sides.

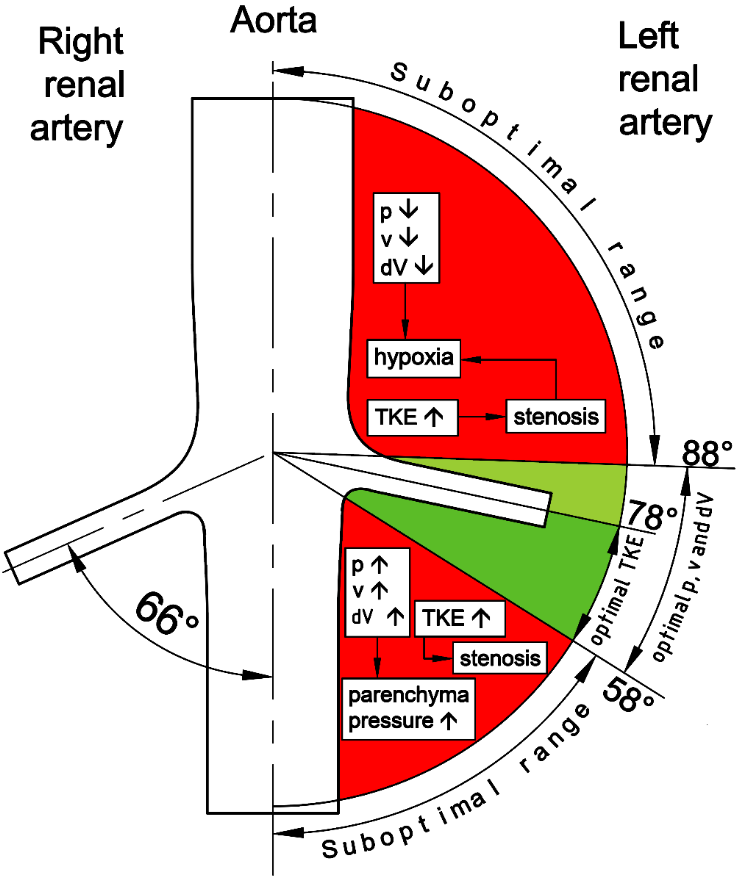

Figure 1. Optimal and suboptimal renal artery branching angles and their fluid dynamics and physiological consequences.

5.5. Effects of hypertension and isolated systolic hypertension on single kidney patients

The results of the simulation series show that hypertension and isolated systolic hypertension increase the difference between the flow characteristics of the healthy and single kidney conditions. Thus, the simulated blood pressure changes are similar in nature, but result in more significant changes in the solitary kidney case.

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