

## LONGITUDINAL CHANGES IN AGE DEPENDENT FREQUENCY-VOLUME CHART REFERENCE VALUES FOR HEALTHY MALES

### Hypothesis / aims of study

Earlier we reported Frequency-Volume Chart (FVC) reference data from healthy male volunteers and a strong age dependence of parameters like (maximum) voided volume, voiding frequency and urine production [1]. Presently we report changes in FVC parameters in a longitudinal follow-up of 719 healthy male volunteers.

### Study design, materials and methods

Between November 2001 and March 2007, 719 healthy male volunteers (age 38-77 at inclusion), all taking part in a non-invasive longitudinal study, were requested to twice complete a FVC for at least 3 consecutive days under normal daily circumstances, including bed and wake up times. The first series of FVC was completed between November 2001 and December 2003 (round 1), the second series was completed approximately 2½ years later, between June 2004 and March 2007 (round 2). Voided volumes were measured using a disposable 1L measuring jug. Study exclusion criteria were a flow rate of less than 5 ml/s, history of any heart condition and treatment or surgery of the lower urinary tract. LUTS were not an exclusion criterion. Several straightforward parameters were calculated from the FVC's: maximum voided volume [ml], mean voided volume during the day [ml], and night [ml], voiding frequency during the day and night and urine production during the day [ml/hour] and night [ml/hour]. Urine production was calculated for each of the 24 hours of each day by linear interpolation of bladder volume between voids and averaged for the number of days that FVC's were kept, assuming the bladder was always completely empty after each voiding [1]. The men were stratified in 8 agegroups. For each agegroup the 5<sup>th</sup>, 50<sup>th</sup> and 95<sup>th</sup> percentile of each FVC parameter was calculated. Then regression analysis was performed of the percentile values on the 8 age groups (figure 1).

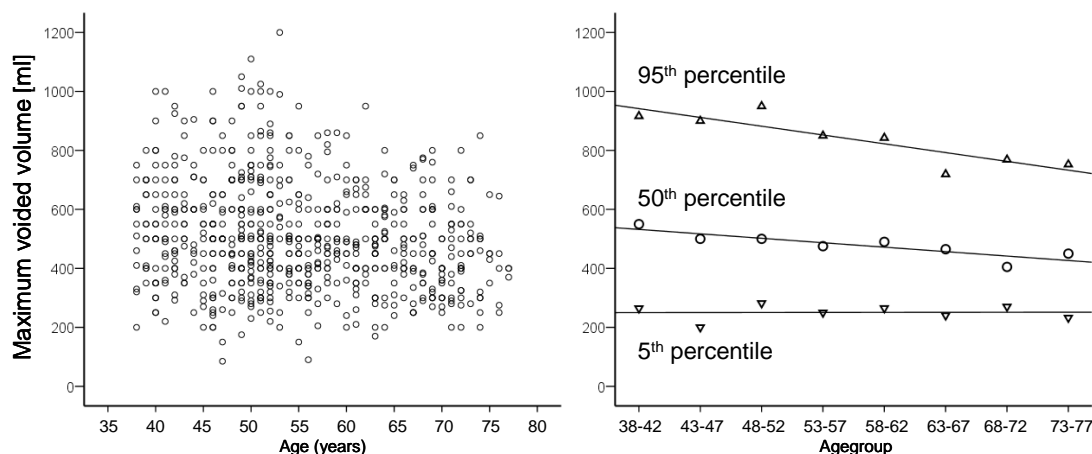


Figure 1 Example of data analysis by regression analysis of the percentiles on the agegroups.

### Results

The numbers of volunteers in the 8 agegroups were 86, 91, 165, 99, 84, 80, 82, 32, respectively. Scatter plots from the FVC parameters versus age showed a distribution of data that could not be described by a single regression line. For example, in figure 1 the range of maximum voided volume decreased with age. It was apparent that the 5<sup>th</sup> percentile did not change with age, whereas the 95<sup>th</sup> percentile decreased from 916 ml at 38-42 years to 753 ml at 73-77 years. Therefore, the age dependent distribution of the FVC parameters was studied by regression analysis of the percentiles on the agegroups.

Table 1 shows both the regression coefficient and slope in round 2 of the, 5<sup>th</sup>, 50<sup>th</sup> and 95<sup>th</sup> percentile of each FVC parameter. In general, the results of round 1 were similar, with the exception of 4 parameters. The 95<sup>th</sup> percentiles of the voided volume both during the day and the night were unchanged with increasing age in round 1, but decreased with increasing age in round 2. The 5<sup>th</sup> percentile of the voiding frequency during the day was comparable in all agegroups in round 1, but increased with age in round 2. The 95<sup>th</sup> percentile of the urine production during the day decreased with increasing age during the first round, but was unchanged in round 2.

Table 1 Regression analysis of frequency-volume chart parameters on agegroups in round 2

	5 <sup>th</sup> percentile		50 <sup>th</sup> percentile		95 <sup>th</sup> percentile	
	R <sup>2</sup>	Slope	R <sup>2</sup>	Slope	R <sup>2</sup>	Slope
Voided volume max	0.000	0.2	0.758*	-15.1	0.762*	-29.8
Voided volume day	0.256	-1.4	0.141	-1.6	0.612*	-7.9
Voided volume night	0.767*	-7.6	0.893*	-11.3	0.874*	-12.0

Frequency day	0.575*	0.10	0.228	0.06	0.134	0.10
Frequency night	-	0	0.906*	0.13	0.881*	0.18
Production day	0.166	-0.7	0.153	-1.0	0.025	-1.0
Production night	0.216	0.7	0.959*	3.6	0.180	2.7

\* P<0.05 significant dependence of FVC parameter on agegroups

#### Interpretation of results

Earlier we found that in the same population of healthy men the range of prostate volumes increased with age [2]. In the present analysis, we find that the age related changes in FVC values are also best described in terms of a change in range. In older men, the range of maximum voided volume values was smaller than in younger men. More accurately, the 95<sup>th</sup> percentile of voided volumes decreased significantly with age, whereas the 5<sup>th</sup> percentile remained constant, effectively reducing the difference of both percentiles. We hypothesize that the men in the older agegroups with a larger prostate volume had on average a higher urethral resistance. This may have led to less effective bladder emptying, resulting in post void residual volume. As a consequence, the bladder will have reached its capacity earlier, resulting in more frequent voidings of smaller volumes. This is supported by the finding that the range of voiding frequencies was smaller in the group of older men, caused by an increase in the 5<sup>th</sup> percentile of the daytime frequency. There was also an increase in the 95<sup>th</sup> percentile of the night time frequency, which is most likely, at least partly, caused by redistribution of body fluid in the night, caused by cardiac decompensation. An alternative or additional explanation for the decrease in (range of) maximum voided volumes with age is that the older men more often had developed an overactive bladder (caused by prostate enlargement), leading to earlier sensation of bladder filling and subsequent voiding at smaller degree of filling. The calculated urine production values in table 1 do not show major changes in range, confirming that there were no major age related changes in fluid intake of this population of healthy volunteers. At night, the calculated urine production values also do not show major changes in range. However, the 50<sup>th</sup> percentile increases with age, which confirms our hypothesis on redistribution of body fluid in the night. The described differences in results of the voided volume and voiding frequency between the first and second study round show generally that in the elapsed period of approximately 2½ years, the voiding of this population of healthy volunteers has worsened.

#### Concluding messages

In older healthy males the range of maximum voided volumes was smaller than in younger males, more specifically by a decrease of the highest maximum voided volumes. This pattern was not seen in the first study round of a longitudinal follow up, but emerged in the second round, done 2½ years later. A third study round has been done in these volunteers and results will follow.

#### References

1. J Urol. 182:210-214 (2009)
2. Urologica. 16:279-288 (2006)

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<b><i>Is this a clinical trial?</i></b>	<b>No</b>
<b><i>What were the subjects in the study?</i></b>	<b>HUMAN</b>
<b><i>Was this study approved by an ethics committee?</i></b>	<b>Yes</b>
<b><i>Specify Name of Ethics Committee</i></b>	<b>Medical Ethical Committee Erasmus MC</b>
<b><i>Was the Declaration of Helsinki followed?</i></b>	<b>Yes</b>
<b><i>Was informed consent obtained from the patients?</i></b>	<b>Yes</b>