the disease in a rural Japanese population. We have performed the survey in Matsudai town Niigara city, Japan since 1979 and the survey was performed every 7 years. In this survey, check-up included an interview, physical examination, anteroposterior standing radiographs of both knees. In this survey, knee OA was defined as being present in a knee if radiographic grade of 2 or higher with Kellgren and Lawrence (KL) scale were detected. In current study, subjects were female ages were between 60 and 80 years who attended the both 4th (2000) and 5th (2007) project of the Matsudai knee OA survey. In 5th survey, we measured urinary N-terminal crosslinking telopeptide of type I collagen (NTx) and C-terminal crosslinking telopeptide of collagen type II (CTX-II) of 564 female aged 60 and older. Occurrence of knee OA was defined if a grade 0 or 1 at the 4th survey advanced to grade 2 or higher at 5th survey. Progression of the disease was defined if a grade 2 at the fourth survey advanced to grade 3 or higher at 5th survey. We compared the data of NTx and CTX-II between occurrence and non-occurrence groups as well as between progression and non-progression groups in age ranged 60-70 year-old and 71-80 year-old. Statistical significance of a difference between two continuous variables tested by Mann-Whitney U test and p-value of less than 0.05 was considered statistically significant.

Results: In younger participants, ages between 60 to 70 years, showed the mean value of CTX-II in non-occurrence and occurrence group were 231±212 (ng/mmolCr) and 315±255 (ng/mmolCr), respectively. The mean value of CTX-II in non-progression and progressive group were 276±246 (ng/mmolCr) and 416±314 (ng/mmolCr). We found occurrence and progression group showed significantly higher value of CTX-II in comparison non-incident or non-progression groups (47% and 50% increase, respectively) in aged between 60 to 70-year-old. In younger participants, incident group and progression group were higher amount of NTX than non-occurrence and progression group, but they are not statistically significant. People older than 71, there is no statistically significant difference in the value of CTX-II as well as NTx between incident and non-incident as well as between progression and non-progression groups.

Conclusions: Currently, there are no available biomarkers which predict the disease progression of knee OA. Current study suggested that CTX-II might be a candidate as an OA incident as well as progression marker especially relatively younger female (60-70 years old) in this retrospective study of Matsudai knee OA survey.

124 IDENTIFICATION OF NOVEL BIOLOGICAL MARKERS OF OSTEOARTHRITIS BY A PROTEOMIC APPROACH

M. Gharbi1, M. Deberg1, J.-E. Dubuc2, E. De Pauw1, Y. Henrotin1
1Univ. of Liege, Liege, Belgium; 2Cliniques universitaires St-Luc, Bruxelles, Belgium

Purpose: A proteomic approach was applied to discover novel osteoarthritis specific biological markers by comparing the protein profile of urines from healthy subjects (C), or patients with osteoarthritis (OA) or osteoporosis (OP).

Methods: Urine samples were collected from 10 women (76±5 years) undergoing knee replacement surgery due to severe OA, four age-matched women with severe osteoporosis (OP) and five young healthy women (C) (25.6±2.6 years) without clinical signs of joint disorders. Proteins were separated by two-dimensional difference gel electrophoresis (2D-DIGE), and the proteins with significantly increased or decreased expression in the OA sample were subject to identification by tandem mass spectrometry.

Results: 19 spots intensity was increased or decreased at least 1.5 times in OA compared to C urine samples (t-test: p < 0.05). Fibulin-3 (Q12805), Zn-α2 glycoprotein precursor (P25311), apop-tosis factor 2 (Q9BRQ8), beta-actin (P60709), AMBP protein precursor (P02760), GP36b glycoprotein (Q12907), polymeric-immunoglobulin receptor (P01833) were found to be increased in OA while serpin B1 (P30740), serpin B3 (P29508), kininogen-1 precursor (P01042), alpha 1 anti-trypsin (P01009), serotransferin (P02787), mannose binding lectin associated serine protease (O00187) decreased in OA patients compared to C. Particularly, five spots containing fibulin-3 sequences were increased (by 4 to 8 fold according the isoform) in urine of patients with OA compared with those of C, but decreased (by 4 to 12 fold according the isoform) in OP urine compared with OA.

Conclusions: Some of the proteins identified are known to be implicated in the inflammatory process, for example, the kininogen precursor or alpha-1-antitrypsin. This observation coincides with the pathology of osteoarthritis. A significant increase in the concentration of specific fibulin-3 fragments was observed in OA subjects compared to C and OP subjects. Functional classification indicates that fibulin-3 is related with skeletal development and its regulation by the interaction with some inhibitors of metallo-proteases. These data suggest that fibulin-3 fragments could be useful biomarkers of OA.