P-267 Characterising a novel embryo grading system for 4-cell embryos including symmetry, fragmentation, cell configuration, cell contacts per cell, distance between cells, and cell adhesion strength

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Study question: What other cell junction factors can be easily characterised from imagery of 4-cell embryos to assist in embryo classification and prediction of viability?

Summary answer: 4-cell embryo grading should not only account for symmetry and fragmentation, but also cell configuration and cell adhesion quality.

What is known already: 4-cell embryos are clinically classified according to cell number, symmetry and fragmentation without accounting for cell orientation or quality of cell junctions. Our previous work has focused on classification of 4-cell embryos according to overall embryo shape ("tetrahedral" versus "planar") using artificial intelligence. Our work, as confirmed by others, has demonstrated that embryo shape at the 4-cell stage is an important determinant of the ability of the embryo to reach blastocyst, utilisation, pregnancy and live birth. This is thought to be because of variations in intracellular communication between cells in embryos with different orientations, and consequently, different intracellular junction phenotypes.

Study design, size, duration: Using geometrical principles, possible permutations of 4-cell embryos (excluding redundant mirrored permutations) were identified and further classified based on shape and number of cell junctions. For ease of calculations, cells were assumed to be spherical, with at least one intracellular cell contact and symmetrical in size with other cells in the same embryo.

Participants/materials, setting, methods: The six distances between centroids of permutations for each configuration were calculated relative to the size of the cell, and the shortest distance between cell membranes. Adhesion was characterised from embryo imagery based on the overall shape of the cell, external angle between cells and the length of cell contact (the more spherical the cell, the larger the angle and the longer the cell contact point, the stronger the adhesion, adapted from Winklbauer,2015).

Main results and the role of chance: 4-cell embryos may be classified into 13 variant configurations: 1 typical Tetrahedral, 2 quasi-tetrahedral, 10 planar. These variants were classified according to number of cells with 0,1,2 and 3 intracellular contacts, leading to six possible configurations: 0004(tetrahedral), 0022(quasi tetrahedral/planar), 0040 (planar), 0121(quasi tetrahedral/planar), 0301(planar), 0220(planar). The number of total cell junctions in the embryo in each of these configurations was 12,10,8,8,6,6 respectively, with tetrahedral embryos (0004) having twice the cell contacts compared to planar embryos ($p<0.001$). Tetrahedral embryos have an advantage over the other embryo configurations in terms of better embryo communication, as demonstrated by the lower average and variation in distance and shorter sum of all intracellular distances between centroids (mean: 0.78 vs 0.94,0.98,1.04,1.09,1.19; stdev:0.06 vs 0.2,0.3,0.3,0.4,0.4,0.3; sum:4.7 vs 5.2,6.3,6.1,6.7,7.0,6.0 cell lengths) and between cells (mean: 0 vs 0.34,0.07,0.39,0.42,0.56; stdev: 0 vs 0.56,0.11,0.51,0.53,0.66; sum: 0 vs 2.71,0.43,3.13,3.38,4.46 cell lengths) observed in tetrahedral embryos versus other five configurations respectively ($p<0.001$).

Cell junctions were classified according to degree of cell adhesion: A:none (cells remain spherical in shape); B:weak (external angle between the cells is acute, there is a narrow visible cell junction); C:strong (external angle between the cells is obtuse with a wide visible cell junction). Limitations, reasons for caution: Follow-up studies will evaluate the impact of different cell shapes,cells without intracellular contact,and asymmetrical embryos. The proposed classification will be validated against a database of known outcome from 8 clinics from 6 countries to quantify the clinical implications of this classification,and the consistency of assessment by humans and AI .

Wider implications of the findings: It is clear that differences in intracellular communication between cells in embryos with different orientations, and different intracellular junction phenotypes is an important determinant of embryo viability. Our classification system allows for an easy to use and mathematically sound criteria for classifying 4-cell embryo cell junction quality.

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